1,5-Dipolar Electrocyclizations of Thiocarbonyl Ylides, a New Approach to Five-Membered Sulfur-Heterocycles

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I would like to express my deepest gratitude to

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To my family

for their constant encouragement, support and guidance throughout my entire education.

Foreword

This Ph. D. thesis is based on the results published or being published in an international scientific journal. It is presented in four chapters corresponding to the papers in as much an unchanged form of the respective manuscripts as possible. Therefore, compounds and references are numbered independently in each chapter. An overview of the entire work is given in the following summary.

CONTENTS

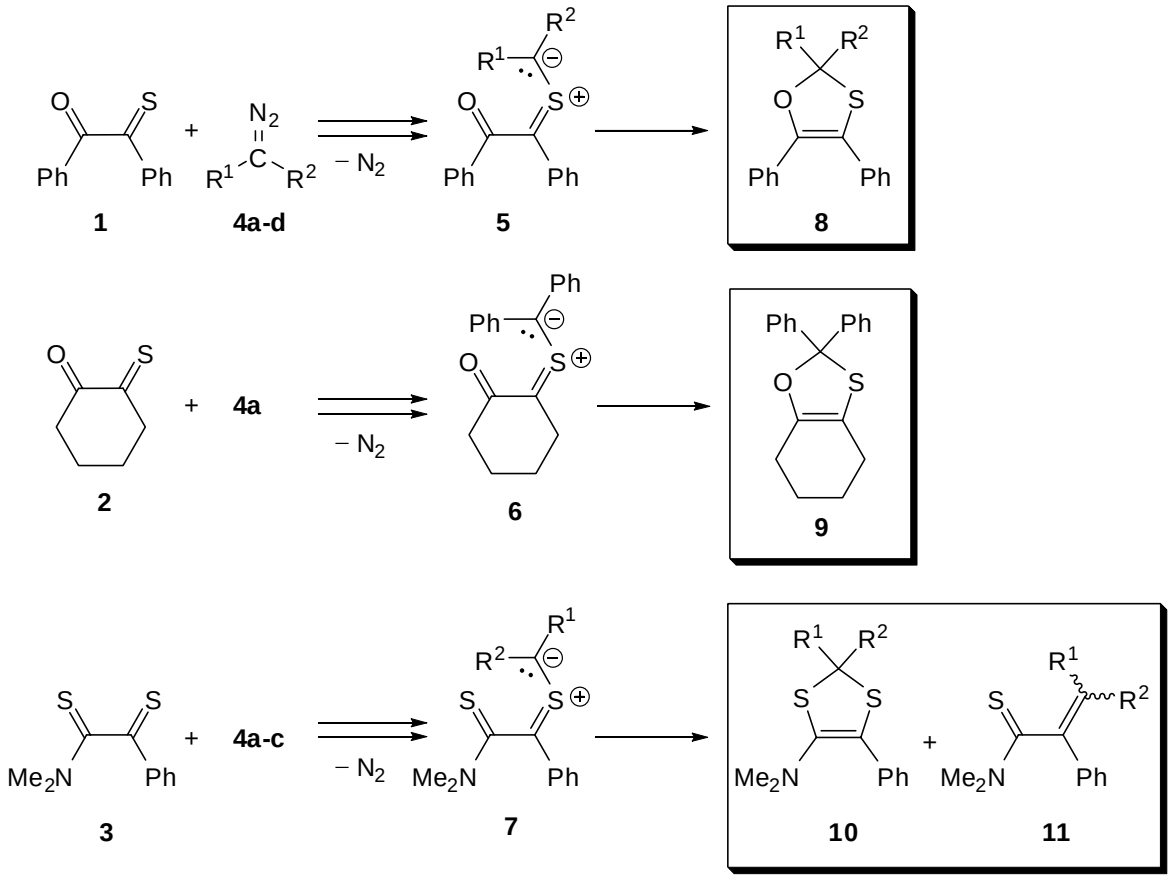
1. Zusammenfassung

In der vorliegenden Arbeit werden Reaktionen von α,β-ungesättigten Thiocarbonyl-Verbindungen mit Diazo-Verbindungen untersucht. Im Zentrum steht einerseits die Isolierung und Identifikation der bei den Umsetzungen gebildeten Produkte und andererseits die Untersuchung und Klärung der Reaktionsmechanismen, welche zu den Produkten führen.

Im Kapitel 4 werden zunächst Umsetzungen von 1,2-Diphenyl-2-thioxoethanon (**1**), dem intermediär gebildeten 2-Thioxocyclohexanon (**2**), sowie *N*,*N*-Dimethyl-2-phenyl-2-thioxothioacetamid (**3**) mit den Diazo-Verbindungen **4a-d** (*Tabelle*) beschrieben.

In allen Reaktionen bildet sich dabei als Zwischenprodukt nach einer 1,3-dipolaren Cycloaddition und anschliessender Cycloreversion unter N_2-Eliminierung das jeweilige Thiocarbonyl-Ylid **5**, **6** bzw. **7** (*Schema 1*).

Schema 1

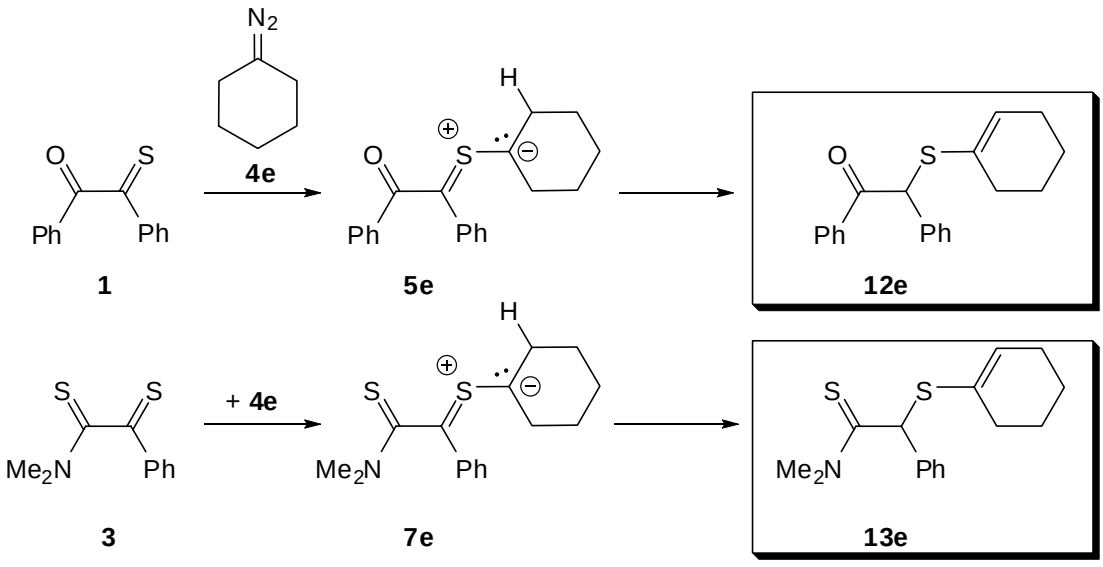


	R^1	R^2
4a	Ph	Ph
4b	Ph	H
4c	4-$MeOC_6H_4$	4-$MeOC_6H_4$
4d	H	H
4e	—$(CH_2)_5$—	
4f	H	CO_2Et

Tabelle

Die Reaktionen von **1** mit **4a-d** führten zu den entsprechenden 4,5-Diphenyl-1,3-oxathiolen **8a-d**, welche *via* eine 1,5-dipolare Elektrocyclisierung des Thiocarbonyl-Ylids **5** gebildet wurden. Nach dem gleichen Mechanismus verliefen auch die Umsetzungen von **2** mit **4a** und von **3** mit den Diazo-Verbindungen **4a-c**. Es wurden dabei das bicyclische 1,3-Oxathiol **9** und die 1,3-Dithiolane **10a-c** gebildet. Als weitere Produkte der Reaktion von **3** mit **4a-c** wurden die α,β-ungesättigten Thioamide **11a-c** isoliert, welche über eine 1,3-dipolare Elektrocyclisierung der Thiocarbonyl-Ylide **7** und anschliessende Elimination von Schwefel entstanden sein dürften. Umsetzung von **1** bzw. **3** mit Cyclohexyl-diazomethan (**4e**) lieferte in beiden Fällen die entsprechenden Thioenolether **12e** und **13e** in relativ guten Ausbeuten. Diese bildeten sich aus den entsprechenden Thiocarbonyl-Yliden **5e** bzw. **7e**, welche über eine [1,4]H-Verschiebung zu den Produkten **12e** und **13e** führten (*Schema 2*).

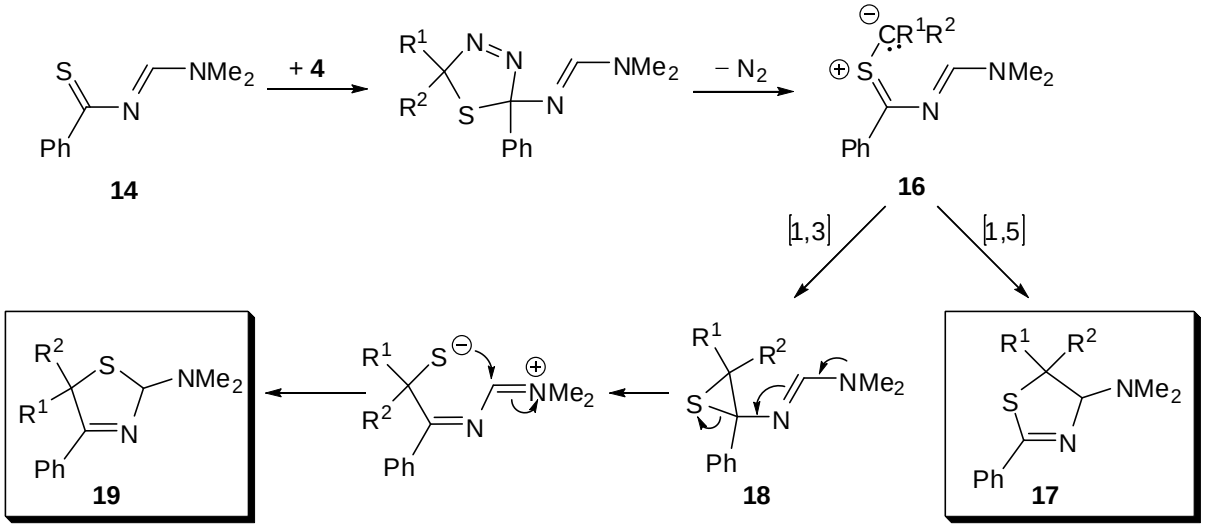
Schema 2



Das Kapitel 5 ist die systematische Fortsetzung von Kapitel 4. Es werden darin Reaktionen von α,β-ungesättigten Thioketonen, welche in der konjugierten Doppelbindung in α- oder β-Position ein N-Atom tragen, mit Diazo-Verbindungen untersucht. Als Edukte dienten *N*-[(Dimethylamino)methylene]thiobenzamid (**14**) und 2-(Dimethylhydrazono)-1-phenyl-ethanethion (**15**).

Die Reaktionen von Thiobenzamid **14** mit **4a**, **4d** und **4e** führten jeweils zu zwei isomeren Hauptprodukten (*Schema 3*). Dabei reagierte **14** zuerst *via* 1,3-dipolare Cycloaddition und anschliessende Cycloreversion unter Abspaltung von N_2 zu den Thiocarbonyl-Ylid-Zwischenprodukten **16**. Letztere stabilisierten sich einerseits *via* eine 1,5-dipolare Elektrocyclisierung zu den entsprechenden 1,3-Thiazolaminen **17** und andererseits *via* eine 1,3-dipolare Elektrocyclisierung zu den jeweiligen Thiiranen **18**, welche sofort in einer Art S_Ni'-Mechanismus unter Ringöffnung zu einem Thiolat reagierten und *via* 5-*exo*-*trig*-Cyclisierung zu den isomeren 1,3-Thiazolaminen **19** führten. Die Ausbeute von **17** war üblicherweise höher als diejenige von **19**.

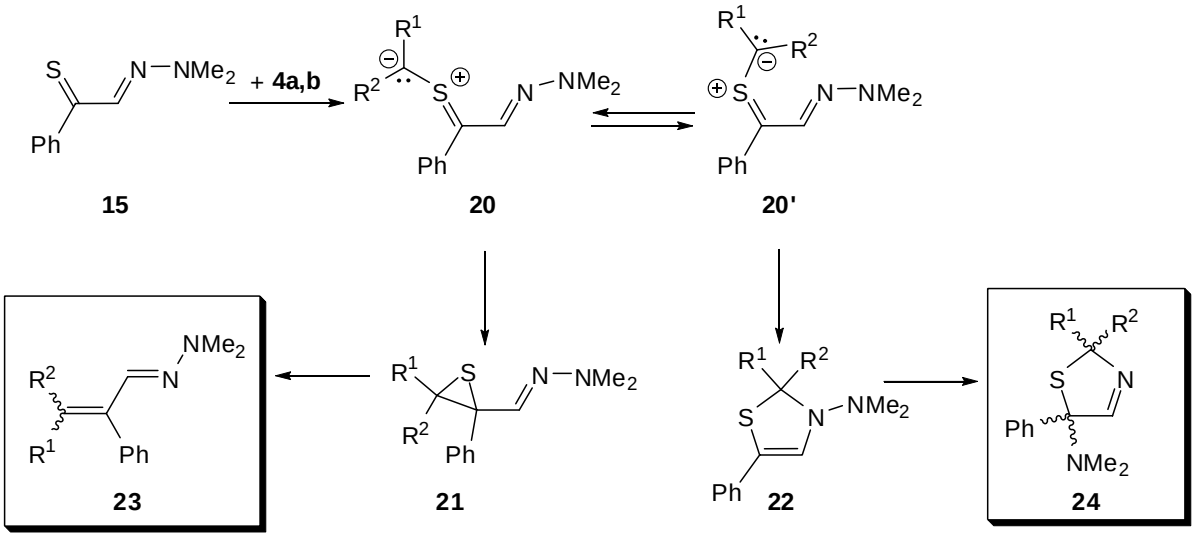
Schema 3



Bei der Reaktion von **14** mit Phenyldiazomethan (**4b**) wurden vier isomere Produkte erhalten, wobei es sich um die jeweiligen *cis*/*trans*-Isomeren von **17b** und **19b** handelte.

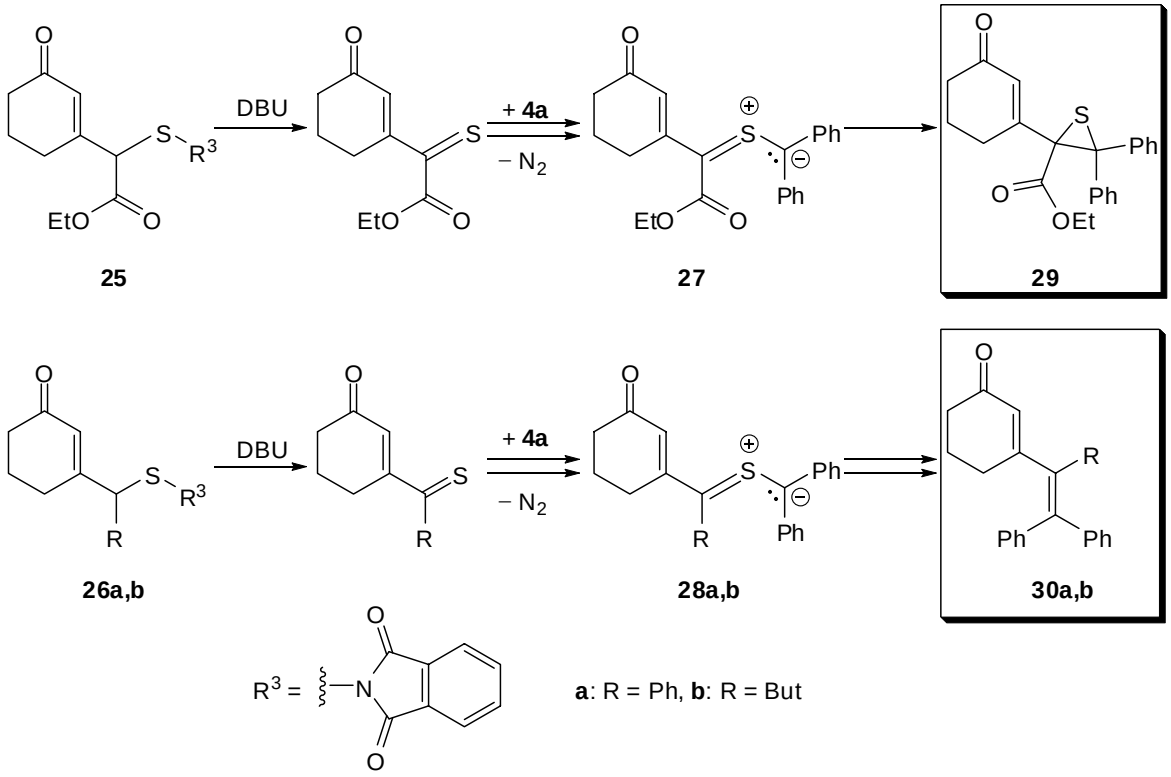
Das Thioketon **15** setzte sich in analoger Weise mit **4a** und **4b** zu den entsprechenden Thiocarbonyl-Yliden **20**/**20'** um. Über eine 1,3- bzw. 1,5-dipolare Elektrocyclisierung reagierten diese zu den Thiiranen **21** bzw. zu den 1,3-Thiazol-*N*-aminen **22**. Isoliert wurden schliesslich die Alkene **23** als Hauptprodukt und die 1,3-Thiazol-5-amine **24** als Nebenprodukt (*Schema 4*).

Schema 4



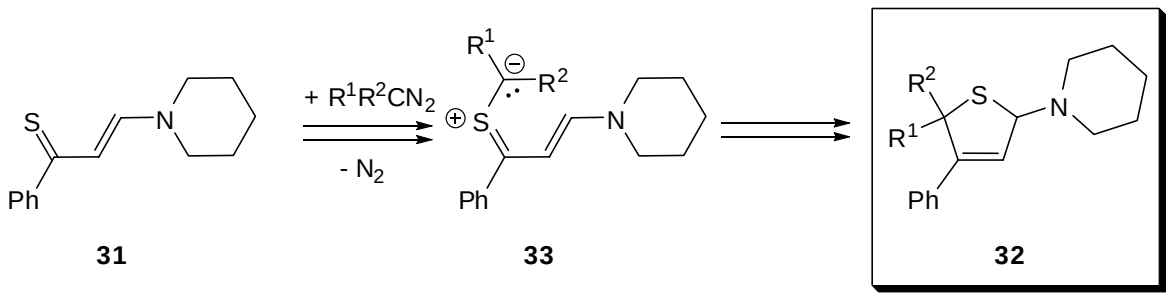
In Kapitel 6 wurden in einem ersten Teil Reaktionen von **4a** mit Thioketonen, welche eine konjugierte C,C-Doppelbindung besitzen, untersucht. Der Zugang zu diesen α,β-ungesättigten Thioketonen ist eingeschränkt, da diese in einer [2 + 4]-Cycloaddition zur Dimerisierung neigen. Um diese zu verhindern wurde die C=S Bindung im letzten Schritt durch eine DBU-katalysierte Reaktion bei tiefer Temperatur aus den Isoindolin-Derivaten **25**, **26a** und **26b** generiert (*Schema 5*). Die dadurch gebildeten α,β-ungesättigten Thioketone reagierten mit **4a** zu den entsprechenden Thiocarbonyl-Yliden **27**, **28a** und **28b**, welche ausschliesslich *via* 1,3-dipolare Elektrocyclisierung zum Thiiran **29** bzw. durch anschliessende Entschwefelung zu den Alkenen **30a** und **30b** führten.

Schema 5



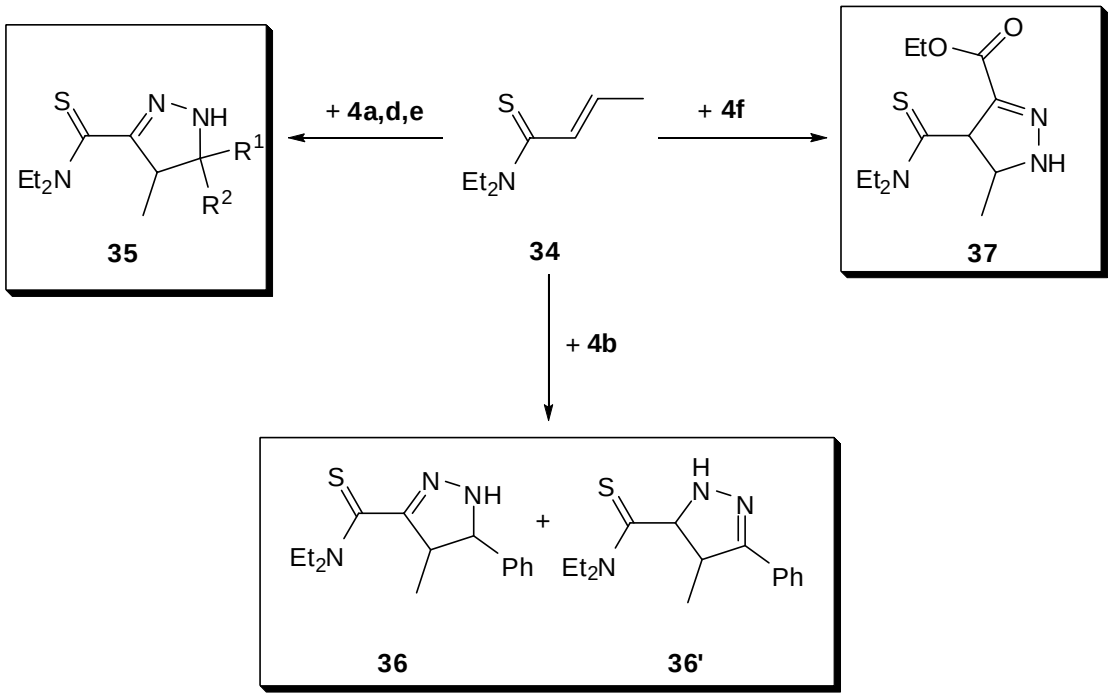
Trägt die konjugierte C,C-Doppelbindung des Thioketons in β-Position noch eine Aminogruppe, so ist die Verbindung auch bei Raumtemperatur stabil und eignet sich somit zur Umsetzung mit verschiedenen Diazoverbindungen. In einem zweiten Teil des Kapitels 6 wurden Reaktionen des vinylogen Thioamids **31** mit **4a**,**b**,**d** und **4e** untersucht. Es wurde jeweils in guter bis sehr guter Ausbeute ein 2,5-Dihydrothiophen des Typs **32** erhalten (*Schema 6*). Diese Verbindungen wurden wahrscheinlich *via* Thiocarbonyl-Ylide **33** gebildet, welche jeweils über Thiirane analog zu dem in *Schema 3* beschriebenen Weg (von **16** nach **19**) gebildet wurden.

Schema 6



Im 7. und letzten Kapitel wurde untersucht, ob α,β-ungesättigte Thioamide mit Diazo-Verbindungen ebenfalls an der C=S Bindung reagieren. Dazu wurde Thioamid **34** mit den Diazo-Verbindungen **4a**,**b**,**d**,**e** und **4f** umgesetzt. Die Ergebnisse zeigten, dass der Angriff der Diazo-Komponente in keinem Fall an der C=S Bindung, sondern ausschliesslich an der C=C Bindung erfolgte. Über eine 1,3-dipolare Cycloaddition und nachfolgende 1,3-H-Verschiebung wurden mit den Diazo-Verbindungen **4a**,**d** und **4e** jeweils die 3-Thiocarboxamide des Typs **35** gebildet. Bei der Reaktion von **34** mit **4b** wurden die tautomeren Verbindungen **36** und **36'** erhalten, welche *via* unterschiedliche 1,3-H-Verschiebung entstanden sind. Sie konnten nach Derivatisierung getrennt und ihre Strukturen bewiesen werden. Bei der Reaktion von **34** mit **4f** wurde als einziges Produkt das regioisomere 4-Thiocarboxamid **37** isoliert. Ein Thiocarbonyl-Ylid-Zwischenprodukt konnte in allen Reaktionen von **34** mit **4** ausgeschlossen werden.

Schema 7



Zusammenfassend kann man sagen, dass grundsätzlich alle Reaktionen von Thiocarbonyl-Verbindungen, die konjugierte π-Systeme aufweisen, mit Diazo-Verbindungen - mit Ausnahme der α-β-ungesättigten Thioamide - über ein Thiocarbonyl-Ylid-Zwischen-produkt verliefen und zu einem grossen Teil auch die jeweiligen 5-gliedrigen Heterocyclen

ausbildeten. Der Mechanismus, der vom Ylid zur Ringbildung führte, ist aber sehr unterschiedlich. 1,5-Dipolare Elektrocyclisierungen sind offenbar dann favorisiert, wenn sich in α- oder β-Position ein elektronegatives Atom (z.B. O, S, N) befindet (Kapitel 4 und 5). 1,3-Dipolare Elektrocyclisierungen sind bevorzugt, wenn in β-Position eine Aminogruppe sitzt (Kapitel 5 und 6).

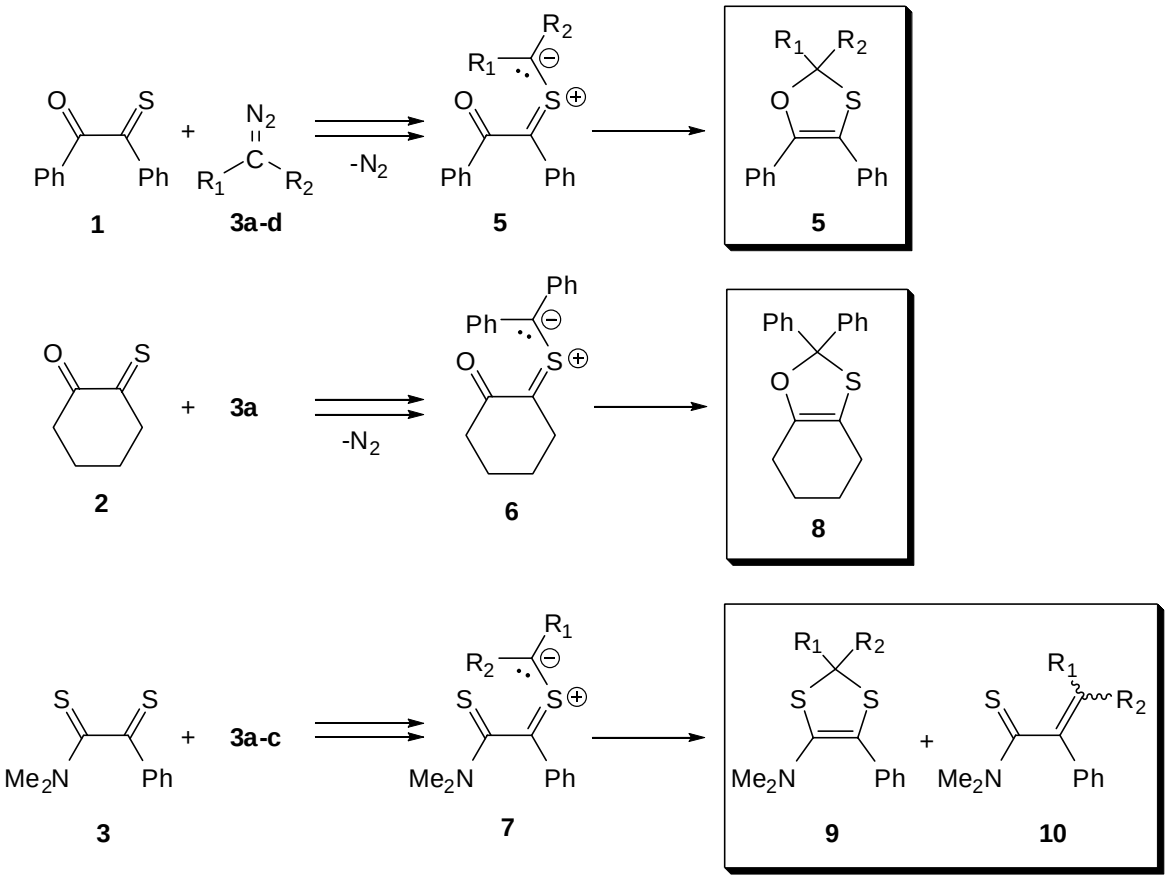
2. Summary

In the present work, reactions of α,β-unsaturated thiocarbonyl compounds with diazo compounds have been investigated. In the center of these investigations there is on the one hand the isolation and identification of the products obtained, and on the other hand the investigation and verification of the reaction mechanisms, which have led to these products.

In Chapter 4, reactions of 1,2-diphenyl-2-thioxoethanone (**1**) and 2-thioxocyclohexanone (**2**), which have been generated as reactive intermediates, and *N*,*N*-dimethyl-2-phenyl-2-thioxothioamide (**3**) with diazo compounds **4a-d** (*Table*) are discussed.

In all reactions, the intermediate thiocarbonyl ylide **5**, **6**, and **7**, respectively, is formed *via* a 1,3-dipolar cycloaddition and subsequent cycloreversion under elimination of N_2 (*Scheme 1*)

Scheme 1

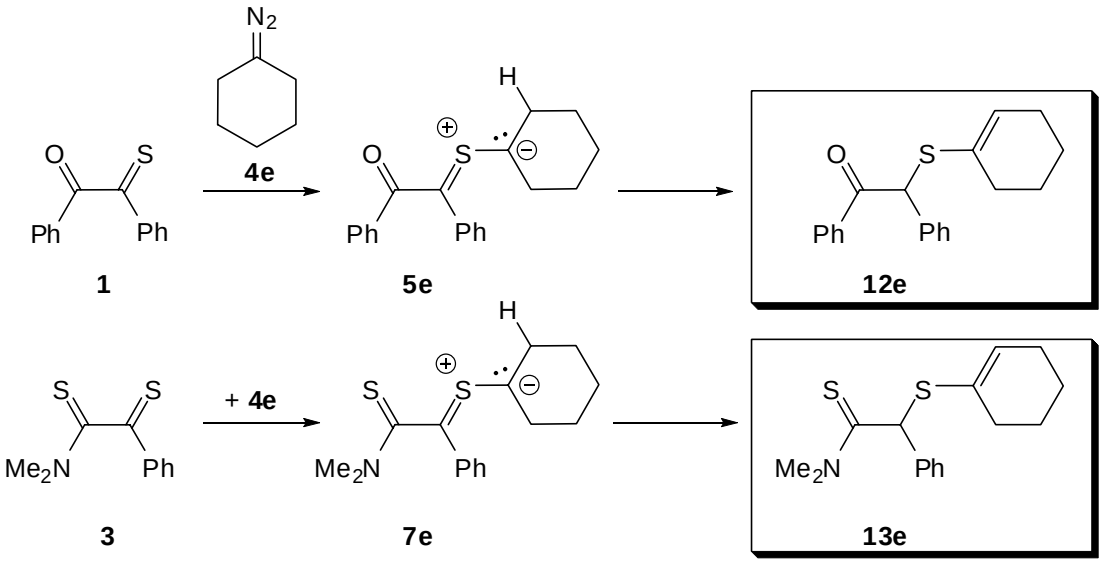


	R^1	R^2
4a	Ph	Ph
4b	Ph	H
4c	4-$MeOC_6H_4$	4-$MeOC_6H_4$
4d	H	H
4e	—$(CH_2)_5$—	
4f	H	CO_2Et

Table

The reactions of **1** with **4a-d** led to the corresponding 4,5-diphenyl-1,3-oxathioles **8a-d**, which were formed *via* 1,5-dipolar electrocyclization of thiocarbonyl ylide **5**. Also the reaction of **2** with **4a** as well as that of **3** with the diazo compounds **4a-c** proceeded *via* the same reaction mechanism, to give the bicyclic 1,3-oxathiole **9** and the 1,3-dithiolanes **10a-c**, respectively. Additional side products, namely the α,β-unsaturated thioamides **11a-c** have been formed most likely by a 1,3-dipolar electrocyclization of the thiocarbonyl ylide **7** and subsequent elimination of sulfur. Conversion of **1** and **3**, respectively with diazocyclohexane (**4e**) led in both cases to the corresponding thioenolethers **12e** and **13e** in relatively good yields, which have been formed by a [1,4]-H shift in the corresponding thiocarbonyl ylides **5e** and **7e**, respectively (*Scheme 2*).

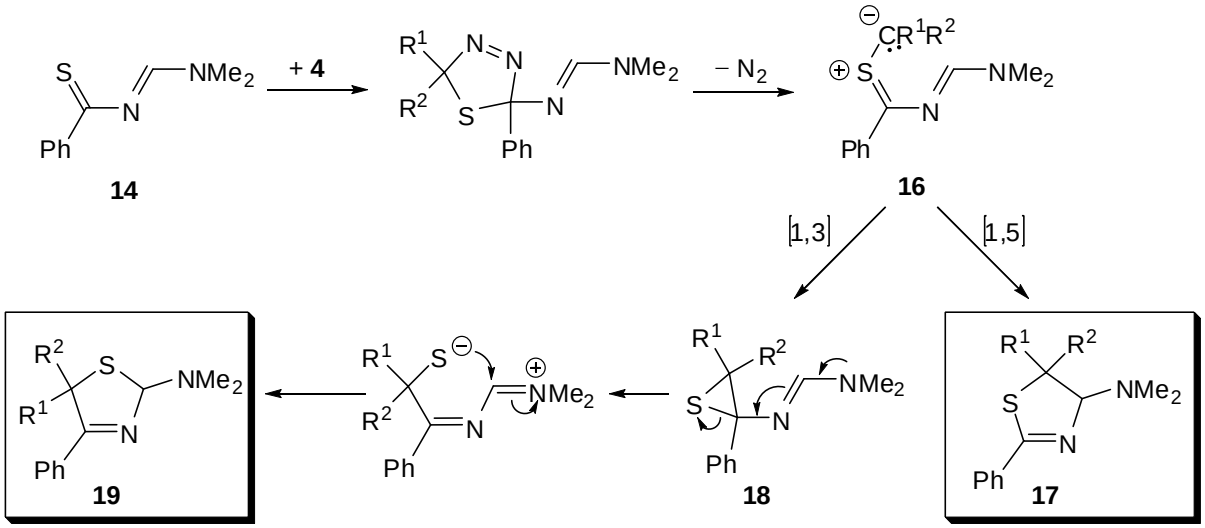
Scheme 2



Chapter 5 is the systematical continuation of chapter 4. It is about the investigations of reactions of α,β-unsaturated thioketones, bearing an N-atom in α- or β-position with diazo compounds. As starting materials *N*-[(dimethylamino)methylene]thiobenzamide (**14**) and 2-(dimethylhydrazono)-1-phenylethanethione were used (**15**).

The reactions of thiobenzamide **14** with **4a**, **4d**, and **4e** led in each case to two isomeric main products (*Scheme 3*). In this process, **14** reacted *via* 1,3-dipolar cycloaddition and subsequent cycloreversion under elimination of N_2 to give the intermediate thiocarbonyl ylides **16**, which were stabilized on the one hand *via* 1,5-dipolar electrocyclization to give the corresponding 1,3-thiazoleamines **17** and, on the other hand *via* 1,3-dipolar electrocyclization to give the respective thiiranes **18**, which, spontaneously reacted in a S_Ni'-like mechanism under ring opening leading to a thiolate, which reacted *via* 5-*exo*-*trig* cyclization to give the isomeric 1,3-thiazolamines **19**. The yield of **17** was normally higher than that of **19**.

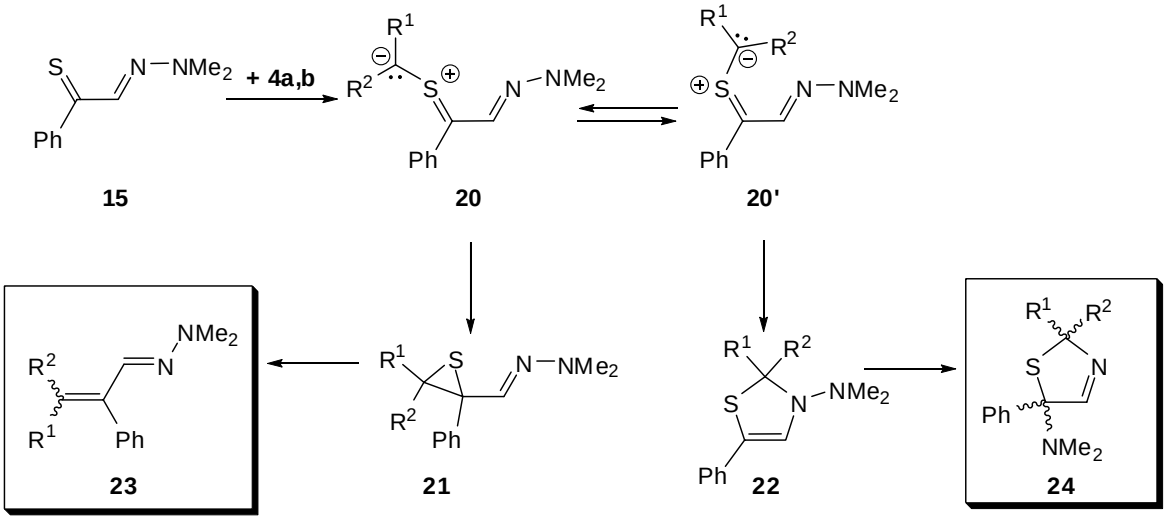
Scheme 3



The reaction of **14** with phenyldiazomethane (**4b**) led to four isomeric products, namely the respective *cis*/*trans* isomers of **17b** and **19**.

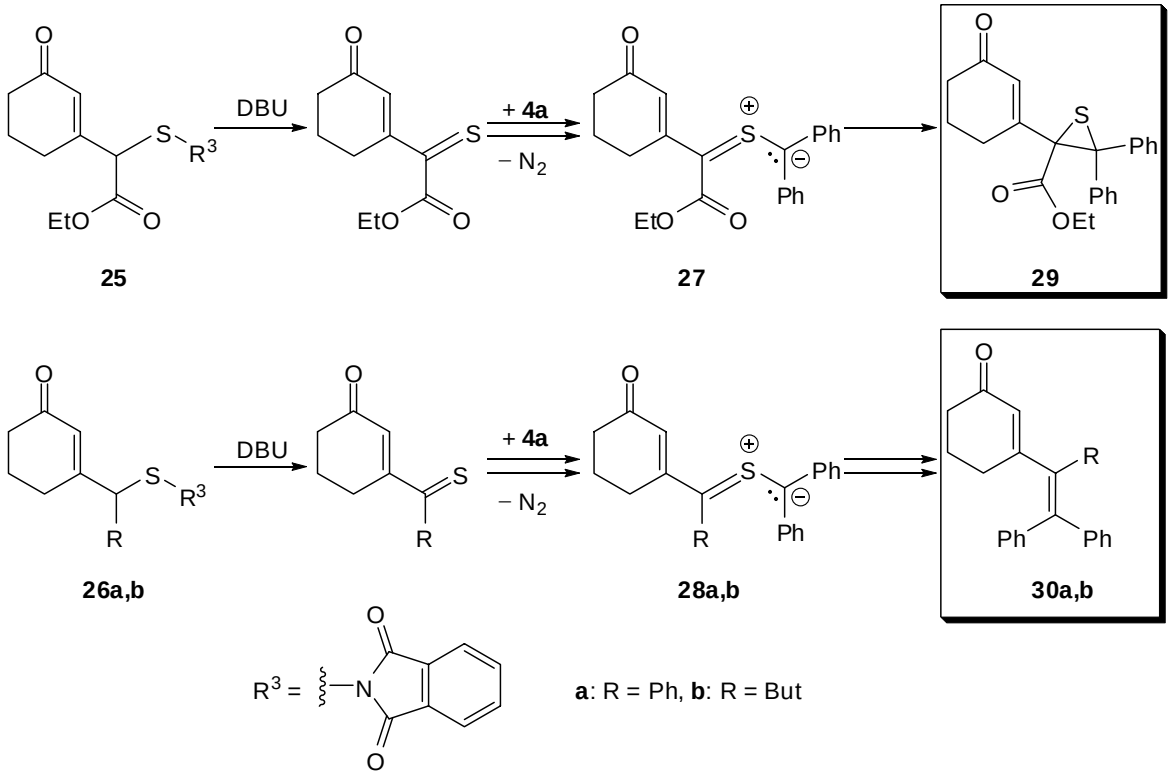
The thioketone **15** reacted with **4a** and **4b** in an analogous way to give the corresponding thiocarbonyl ylides **20**/**20'**, which reacted either *via* 1,3-dipolar or 1,5-dipolar electrocyclization to give the thiiranes **21** and the 1,3-thiazole-*N*-amines **22**, respectively. In conclusion, the alkenes **23** were isolated as main products and the 1,3-thiazole-5-amine **24** could be isolated as minor products (*Scheme 4*).

Scheme 4



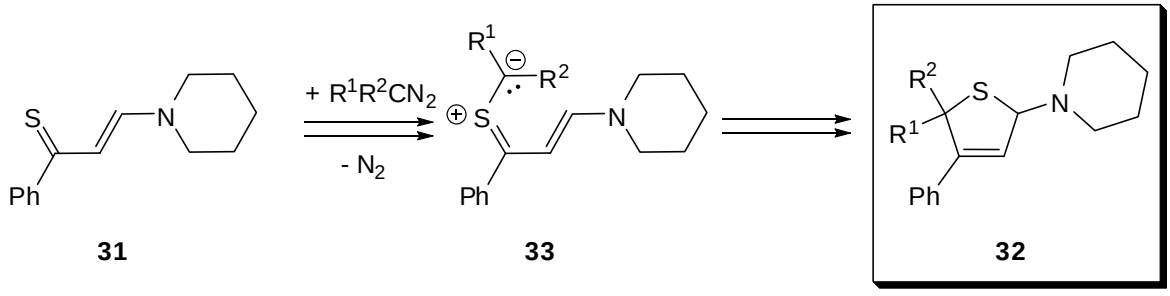
In the first part of chapter 6, reactions of **4a** with thioketones, possessing a conjugated C,C-double bond were investigated. Since α,β-unsaturated thioketones tend to dimerization *via* [2 + 4] cycloaddition, the synthetic approach to such thioketones is remarkably restrained. To avoid this dimerization, the C=S bond was formed in the last step by a DBU-catalyzed reaction at low temperature starting with the isoindoline derivatives **25**, **26a** and **26b** (*Scheme 5*). The *in situ* prepared α,β-unsaturated thioketones reacted with **4a** to give the corresponding thiocarbonyl ylides **27**, **28a** and **28b**, which led *via* 1,3-dipolar electrocyclization exclusively to the thiirane **29** and by subsequent desulfurization to the alkenes **30a** and **30b**, respectively.

Scheme 5



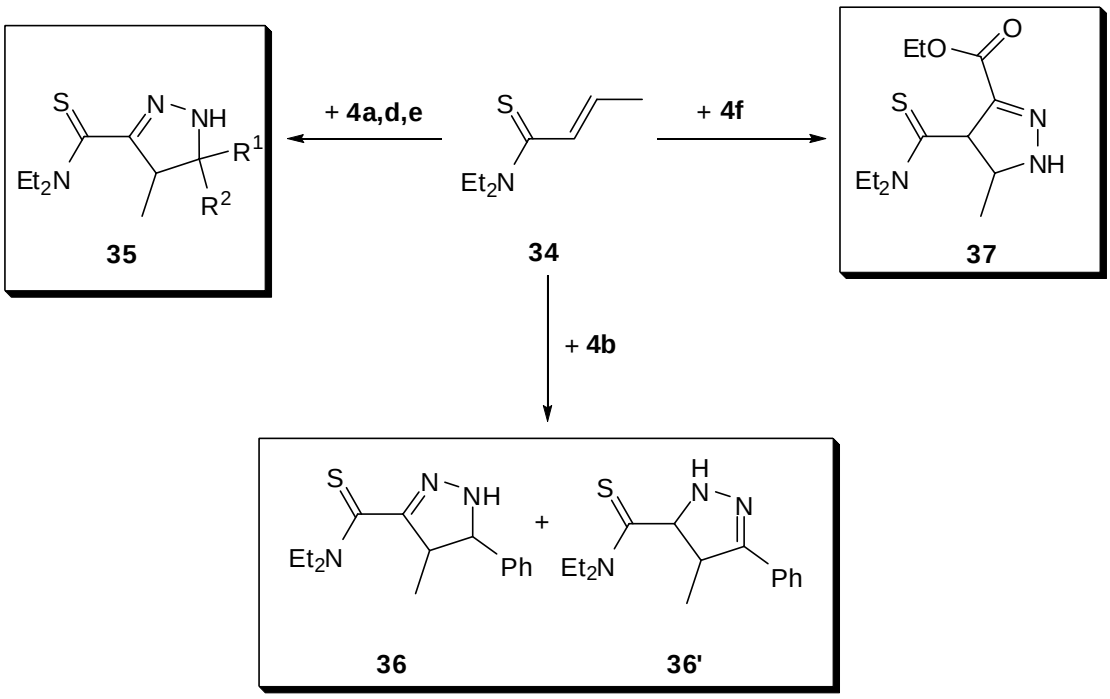
If there is an amino group in β-position to the α,β-unsaturated thioketone, the compound is stable even at room temperature and is therefore suitable for conversions with different diazo compounds. In the second part of chapter 6, reactions of the vinylogous thioamide **31** with **4a**,**b**,**d** and **4e** were investigated. In each case, a 2,5-dihydrothiophene of type **32** was obtained in good to very good yield (*Scheme 6*). These compounds were probably formed *via* the thiocarbonyl ylides **33**, which were obtained from thiiranes in an analogous way depicted in *Scheme 3* (from **16** to **19**).

Scheme 6



In the 7th and last chapter, the investigations concerned the question whether the reaction of α,β-unsaturated thioamides with diazo compounds also occurse at the C=S bond. Therefore, thioamide **34** was reacted with the diazo compounds **4a**,**b**,**d**,**e** and **4f**. The results show that the C=S bond was not involved in the attack of the diazo compound, but in all cases the C,C-double bond was attacked first. The resulting 3-thiocarboxamides of type **35** were formed *via* a 1,3-dipolar cycloaddition of **34** with the diazo compounds **4a**,**d** and **4e** and a subsequent 1,3-H shift. The reaction of **34** with **4b** led to the tautomeric compounds **36** and **36'**, which were formed *via* two different 1,3-H shifts. It was possible to characterize their structures unambiguously after derivatization. In the reaction of **34** with **4f**, the only product was the regioisomer 4-thiocarboxamide **37**. A thiocarbonyl ylide intermediate can be excluded in all cases of the reactions of **34** with **4**.

Scheme 7



In summery, we have shown that essentially all reactions of thiocarbonyl compounds possessing a conjugated π-system with diazo compounds - with the exception of α,β-unsaturated thioamides - reacted *via* an intermediate thiocarbonyl ylide and most of them led to five-membered heterocycles. But the mechanisms, leading to the five-membered ring are indeed very different. The 1,5-dipolar electrocyclization is apparently favored,

when the α- or β-position is occupied by an electronegative atom (i.e. O, S, N) (chapter 4 and 5). If in β-position an amino group is situated, the 1,3-dipolar electrocyclizations are favored (chapter 5 and 6).

3. General Introduction

Sulfur compounds are an essential part of today's chemistry. They are omnipresent in every day's life to the chemical industry. We often come in contact with them also in the kitchen, since the characteristic smells of garlic, onion, bear's garlic, chives or even coffee are due to sulfur compounds (*Fig. 1*).

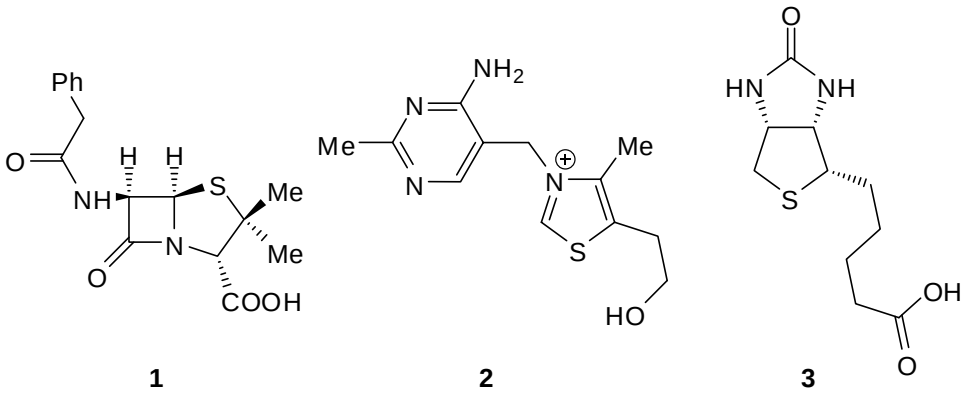
Fig. 1a) *garlic,* b) *bear's garlic*
(Taken from: a) http://de.wikipedia.org/wiki/Knoblauch and
b) http://de.wikipedia.org/wiki/Bild:Baerlauch_Bluete01.jpg)

In industry, sulfuric acid is one of the 20 most important bulk chemicals, used for the synthesis of thousands of other compounds. It is mainly produced by the so-called *Claus process* [1] from hydrogen sulfide, which is renowned for its foul smell of rotten eggs. Sulfur compounds not only have a very strong smell, but also fascinate with a diversity of colors. While elementary sulfur is yellow (*Fig. 2a*)), its color changes to dark red by melting. Compounds of alumosilicate that contain sulfur, for example $Na_4[Al_3Si_3O_{12}]S_3$, have a deep blue color and these rocks are called *Lapislazuli* (*Fig. 2b*)). In some of the compounds described in this work, the multitude of colors due to sulfur compounds is revealed.

a)  b) 

Fig. 2a) *Elementary Sulfur and* b) *Lapislazuli ($Na_4[Al_3Si_3O_{12}]S_3$)*
(Taken from: a) http://en.wikipedia.org/wiki/Image:Sulfur.jpg and
b) http://www.gemstone.org/gem-by-gem/german/lapis.html)

Sulfur was of great importance in ancient medicine. It was prescribed in the past as a laxative (i.e. as a purgative). Another important role was its use against acne. Today, sulfur compounds and especially sulfur heterocycles play an important role in medicine and biochemistry. It was in 1928 that Alexander Fleming discovered an important group of natural sulfur compounds – the penicillins. Although in the recent years, due to increased resistance of bacteria strains towards this type of antibiotics [2], their use has been somewhat reduced, penam-anitibiotics of type **1** (*Fig. 3*, here penicillin G) are still of importance in today's medical treatment of infections [3]. A few other important sulfur-containing heterocycles are thiamin (**2**, Vitamin B_1), which acts as a co-enzyme in the metabolism of carbohydrates [4] and biotin (**3**, Vitamin H), which is a co-enzyme in the citric acid cycle as well as in the fatty acid synthesis [5, 6] (*Fig. 3*).



1 **2** **3**

Fig. 3 *Important sulfur heterocycles: pencillin G* (**1**)*, thiamin* (**2**)*, biotin* (**3**)

The list of important sulfur containing heterocycles could be extended endlessly, which furthermore shows that these compounds are an important branch of synthetic organic chemistry.

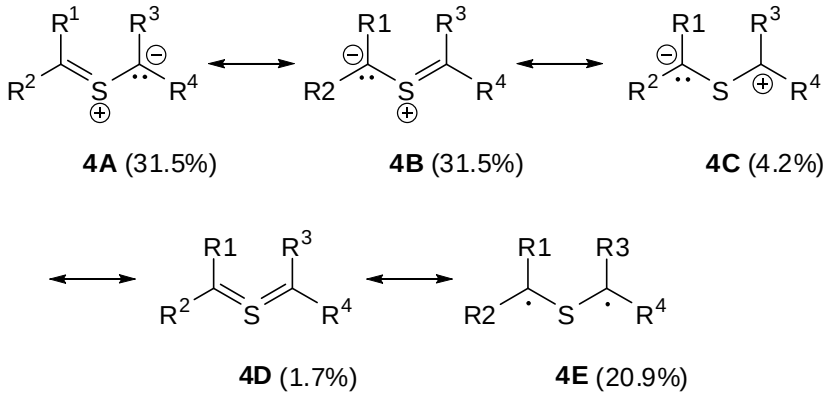
3.1. On the Way to Sulfur Heterocycles

Many types of sulfur containing heterocycles are known, but the ways for their synthesis are even more plentiful. In this work, we will limit ourselves to those synthetic pathways, which include a thiocarbonyl ylide **4** (*Scheme 1*) as an intermediate.

3.1.1. Thiocarbonyl Ylides

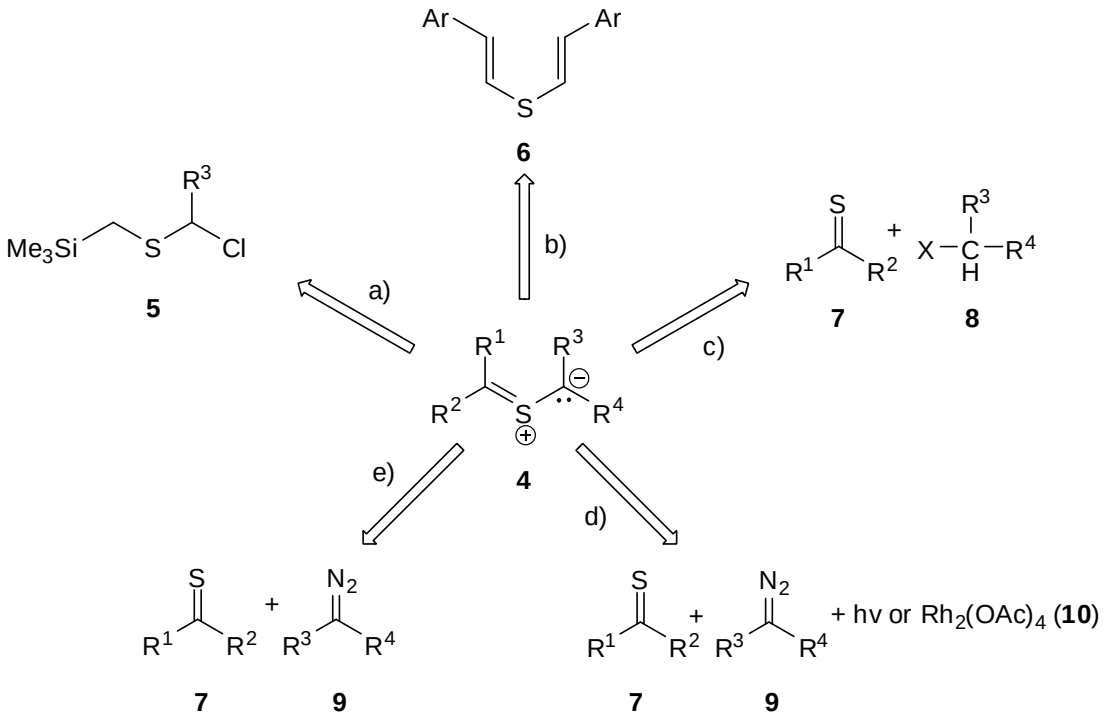
Thiocarbonyl ylides (**4**) are reactive intermediates with a general structure as shown in *Scheme 1*. The different resonance structures **4A-4E** are a result of calculations with the so-called *natural resonance theory* (NRT) and show that the weighting of the structures is quite different (*Scheme 1*) [7]. Although structure **4C** is the one revealing the 1,3-dipolar character of the molecule, its weighting is quite low, with 4.2% only. Structures **4A** and **4B** are, on the other hand, well represented with 31.5% each, which explains why this is the usual manner, in which the species is depicted in literature.

Scheme 1



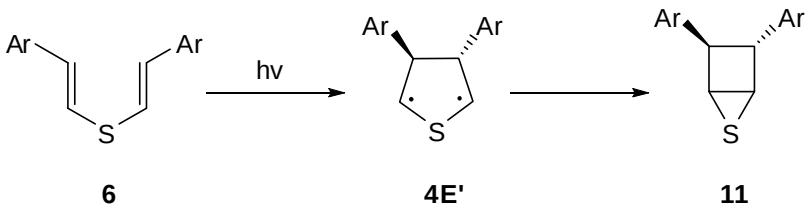
Thiocarbonyl ylides may be synthesized in many different ways (*Scheme 2*). The resulting intermediates are by no means stable and, therefore, their structures are indirectly proven by trapping reactions. Some of these reactions will be discussed in detail in the next sub-chapters (for reviews see [8] and [9]).

Scheme 2



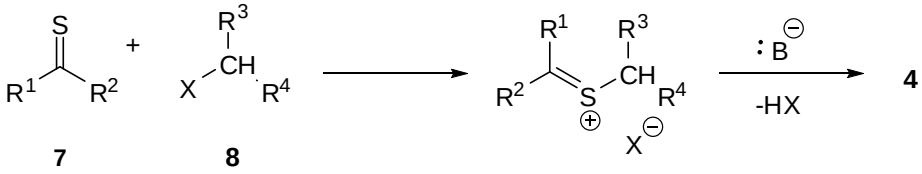
Pathway a) shows an easy synthetic route to substituted thiocarbonyl ylides. Me_3SiCl is eliminated from **5** at room temperature by treatment with fluoride ions. With this method, it is possible to synthesize also the simplest representative of **4** with R^1, R^2, R^3, R^4 = H [10]. Pathway b) describes the photochemical reaction of divinyl sulfides **6**. It is presumed that also in this case a thiocarbonyl ylide **4** is an intermediate of the reaction, for the product of the reaction is the thiirane **11**, the formation of which could be explained by an intramolecular recombination of the two radical-centres in the resonance structure **4E** (*Scheme 1*), leading to the formation of the single C,C bond (*Scheme 3*)[11].

Scheme 3



Another reaction leading to **4** is the deprotonation of sulfenium ions **12** (pathway c)), which are readily available by alkylation of thiocarbonyl compounds **7** with secondary halogenides **8** (*Scheme 4*).

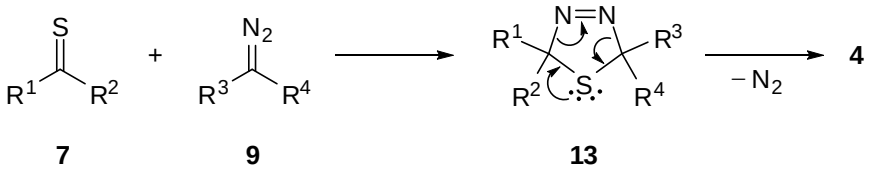
Scheme 4



Carbenes and carbenoïds are often used for the synthesis of 1,3-dipoles by their reaction with nitriles, imines or carbonyl compounds. In the case of thioketones, this pathway allows for the synthesis of **4**. The preparation of the carbenes themselves from the diazo compound could be achieved by photolysis or metal-catalyzed decomposition (pathway d), *Scheme 2*). The latter, especially with $Rh_2(OAc)_4$, is much preferred in small scale organic synthesis.

Pathway e) describes the thermal reaction of thioketones **7** with diazo compounds **9**. The reaction has been intensively investigated by *Schönberg*, *Huisgen*, *Mlostoń* and *Heimgartner* [12-14]. A 1,3-dipolar cycloaddition of the diazo compound to the C,S double bond takes place to give the 2,5-dihydro-1,3,4-thiadiazole **13**. The latter is normally not stable at room temperature and, therefore, a cycloreversion under release of N_2 takes place to give **4** (*Scheme 5*).

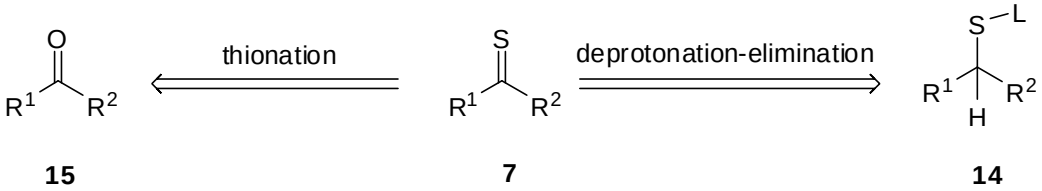
Scheme 5



3.2. Thioketones

Comparing the synthesis of ketones and thioketones, the latter normally is much more complicated than the usually simple way to ketones. The reactions employed to achieve the synthesis of thioketones are divided in two different strategies shown in *Scheme 6*. Often, there is more than one step needed and some sulfur-analogues are accessible only *in situ*. Since enolisable thioketones undergo fast trimerisation it is almost impossible to prepare them in pure form [15]. Only if the enolisable thioketones are sterically hindered there is a real chance for their isolation [16].

Scheme 6

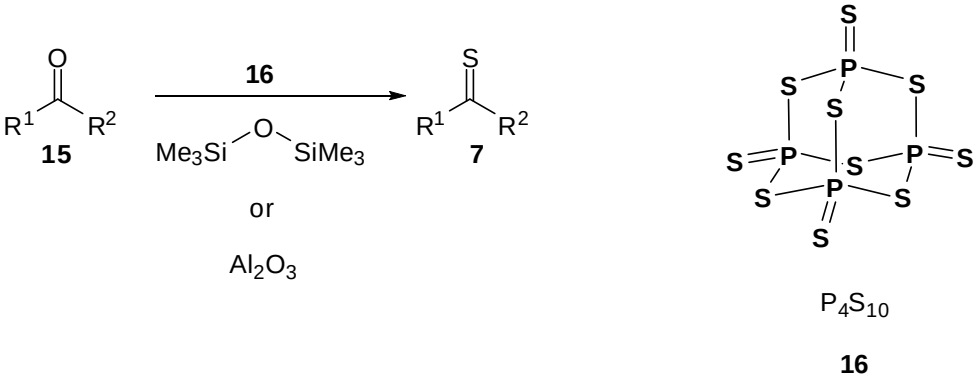


15 **7** **14**

On the one hand, there exists a wide range of reagents and reagent-combinations for the thionation of ketones giving the corresponding thioketones. The number of these reagents is rising from year to year. Therefore, only the most popular thionation conditions are discussed:

a) With P_4S_{10} (**16**): The formation of thioketones by using **16** can be called the classic thionation [17]. The advantage of this method is first of all the wide range of applications and secondly the relatively low price of the reagent. Normally, **16** is used in an apolar or polar, aprotic solvent like toluene, xylene or HMPA. The reaction time until total conversion of the starting material depends on the substitution pattern of the ketone. Further developments of this method by *Curphey* have solved some problems in work up by adding an equimolar amount of hexamethyldisiloxane (HMDO). This remarkably simplifies the work up procedure since the side products are removed just by an aqueous extraction [16]. *Polshettiwar* and *Kaushik* have shown that also the addition of Al_2O_3 has some advantages in work up as simple filtration eliminates a large amount of side products [18] (*Scheme 7*).

Scheme 7



b) With *Lawesson*-reagent (**17**): Since the yield of thionations with **17** is in general good to very good and the application is very simple, today, thionation of ketones with **17**

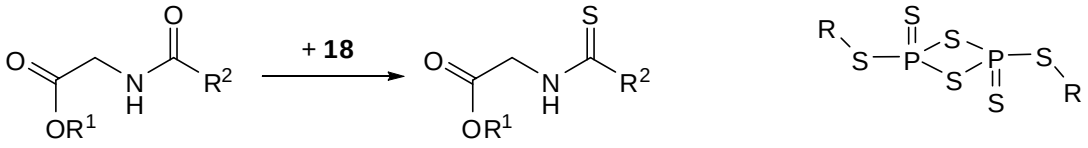
is the most often used method [19] (*Scheme 8*). Sometimes the separation of product and side product is not as easy as it would be desired.

Scheme 8

Lawesson-reagent (**17**)

c) With *Davy*-reagent (**18**) [20]: By comparison of reactions of C,O-double bonds with either **17** or **18,** the results show that in some applications the *Lawesson*-reagent is less suitable in comparison with the *Davy*-reagent (**18**). Namely, in the selective thionation of amides of type **19**, having a ketone or ester group in the same molecule, the *Davy*-reagent is preferably used instead of **17** [21] (*Scheme 9*).

Scheme 9



19 **20**

Davy-reagent (**18**)

R = Me, Et, Tol

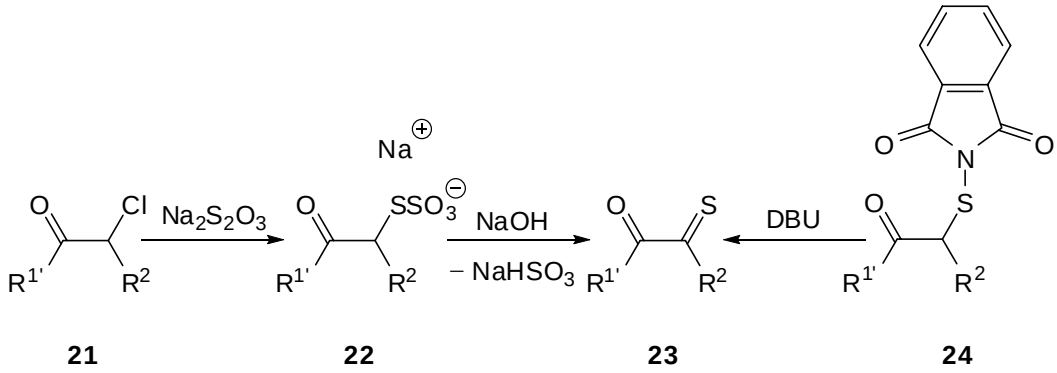
d) If there are especially smooth conditions needed, it is possible to add catalytic amounts of activating reagents to the reaction, whereby high temperature can be avoid. An example has been described by *Capperucci et al.*, in which they used a catalytic amount of TMSOTf and an equimolar amount of hexamethyldisilylthiane (HMDS) [15], wherewith they were able to achieve the thionation of ketones at room temperature.

e) With H_2S/HCl: If the starting material is not acid-sensitive, there is also the option of using a mixture of HCl-gas and H_2S [22] whereby the apparatus complexity and the cost only make sense if other methods have failed.

On the other hand, thioketone **7** is also accessible *via* a deprotonation-eliminination mechanism if there is a convenient leaving group bounded to the sulfur atom (*Scheme 6*). Following this way, also more sensitive thioketones which are not accessible by using

thionation conditions are available, however, these thioketones normally are stable in solution only. Common leaving groups are rare and often restricted to a few applications. Two of them are described in the following (*Scheme 10*). With α-chloroketone **21** and $Na_2S_2O_3$, in a mixture of MeOH and water, the thiosulfat ion **22** can be generated, which reacts with aqueous NaOH under elimination of the sulfite ion to give the α-thioxoketone **23**. A second example is the reaction of isoindole-1,3-dione **24** with DBU [23]. The leaving group in this case is the phthalimide ion.

Scheme 10



3.3. Diazo Compounds

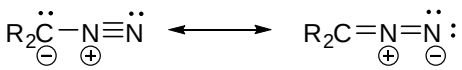
Since diazo compounds play a decisive role in the formation of thiocarbonyl ylides, it is worth to specify the character of these compounds.

3.3.1. Diazoalkane Structure

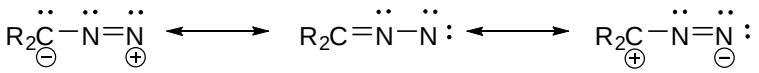
On the basis of their reactivity, diazoalkanes belong to the 1,3-dipoles. But if the different resonances structures of diazoalkanes are described by the valence-bond-theory, it turns out that only the sextet resonance structures, which offend against the octet rule, can correctly illustrate the reactivity as a 1,3-dipol (*Scheme 11*).

Scheme 11

Octet Resonace Structures



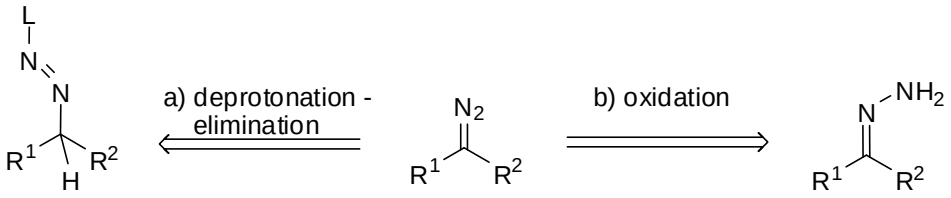
Sextet Resonace Structures



3.3.2. Formation of Diazoalkanes

Since diazo-compounds are generally not stable in pure form and tend to decompose simultaneously under elimination of nitrogen, they are usually stored in solution [24-26]. Diazomethane (**25**) is highly explosive even at –78°C, and that is why its synthesis in pure form is to be avoided [29]. There are two main synthetic ways for the synthesis of diazo-compounds (*Scheme 12*).

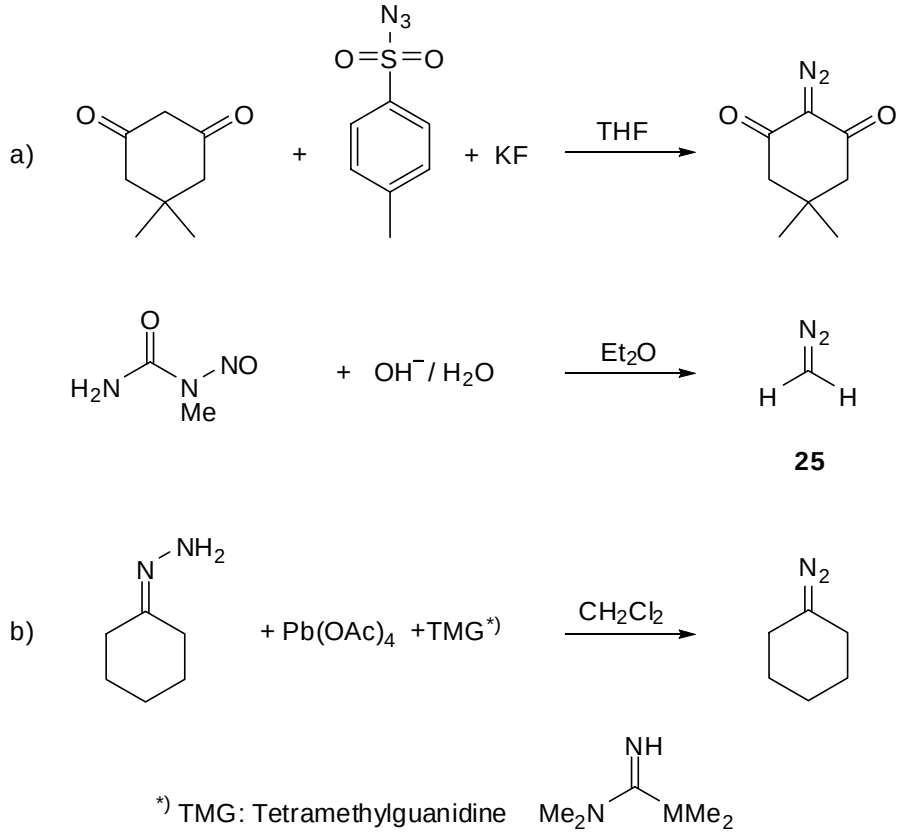
Scheme 12



In pathway a) the α-C-atom to the N,N-double bond is deprotonated and a leaving group, L, is eliminated. In this case the diazo component might be synthesized from an azide and this is indeed a popular method in organic synthesis [27] (*Scheme 13*).

A second possibility offers the oxidation (pathway b)) of hydrazines. Commonly used oxidants are HgO [25] and $Pb(OAc)_4$ [26], but other agents, such as MnO_2 and Ni_2O_3 are also used (for a review see [28]). In *Scheme 13,* a typical example for each pathway is shown. In the case of the formation of diazomethane (**25**), the 'leaving group L' is formed in a rearrangement process [29, 30] and, therefore, it is not a typical representative of compounds synthesized by pathway a).

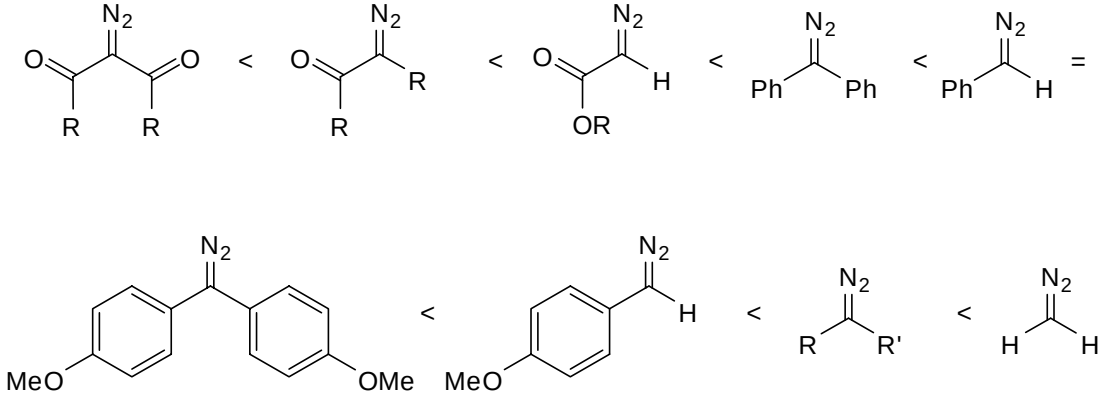
Scheme 13



3.3.3. Reactivity of Diazoalkanes

The reactivity of diazo compounds depends strongly on the reaction partner. Diazomethane (**25**) is a perfect reagent for reactions with carboxylic acids to give methyl esters, since the by-products are gases. In the presence of electron-poor dipolarophiles, a 1,3-dipolar cycloaddition is possible (see chapters 4-7). The first 1,3-dipolar cycloaddition with diazo compounds goes back to 1888, when *Bucherer* reacted ethyl diazoacetate with esters of α,β-unsaturated carboxylic acids [31]. Since then, a variety of diazo compounds have been discovered, and the reactivity of some of them towards dipolarophiles increases in the following order (*Scheme 14*):

Scheme 14



If the already mentioned substrates are not present, the insertion of a CH_2-group into a NH-bond is nowadays possible under $Rh_2(OAc)_4$ catalysis. The reaction proceeds *via* a carbenoïd intermediate, which then reacts with the substrate to form the desired product [32].

3.4. Reaction Mechanisms

Since a lot of the presented reactions proceed *via* one or more pericyclic reactions, it seems to be reasonable to give a short overview of the most common reactions of this class.

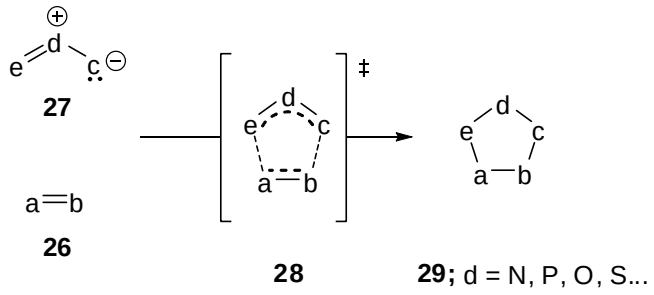
3.4.1. Pericyclic Reactions

Pericyclic reaction proceed in concerted manner *via* a cyclic (or so called pericyclic) transition state. The stereochemistry of those reactions depends on the number of electrons involved. The reactions are classified as follows: cycloadditions, electrocyclizations, sigmatropic reactions, ene reactions, and cheletropic reactions [33]. All of them obey the *Woodward-Hoffmann* rules [34].

3.4.2. 1,3-Dipolar Cycloaddition

Like the *Diels-Alder* reaction, 1,3-dipolar cycloadditions belong to the pericyclic reactions and follow the *Woodward-Hoffmann* rules. 1,3-Dipolar cycloadditions are reactions of dipolarophiles **26** and 1,3-dipols **27**, which pass a cyclic transition state **28** to give the corresponding five-membered ring **29** containing at least one heteroatom (d) (*Scheme 15*).

Scheme 15

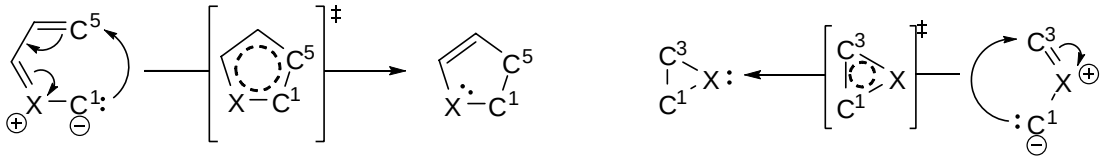


The reaction normally proceeds stereoselectively *cis* whereas the stereochemistry of a two step reaction in a not concerted manner depends on the substituents [35]. If a, b, c, d, and e, respectively, are different or bear different substituents, regioisomers can be formed as the result of different transition states, but often only one isomer is formed due to ideal HOMO-LUMO-relationship of the starting materials.

3.4.3. Electrocyclization

Electrocyclizations are pericyclic ring-closing reactions, which proceed over a cyclic transition state (see 3.4.1.). The number of electrons involved in the reaction is decisive for the stereochemistry of the resulting products. Common reaction conditions are relatively high temperature or irradiation, depending on whether a disrotatory ore conrotatory ring-closure is preferred. Charged systems normally react faster than uncharged-ones [36]. In the present work 1,5-dipolar and 1,3-dipolar electrocyclizations are of particular importance. The indicated numbers 1,5 and 1,3, respectively, indicate the atoms in the chain, which will be connected during the reaction (*Scheme 16*).

Scheme 16



3.5. Aim of the Work

The aim of the presented work was to investigate a fundamental approach to five-membered, sulfur containing heterocycles *via* the reaction of α,β-conjugated thioketones with diazo compounds as described in a few examples [25]. Possible mechanisms are to be discussed and the formation of unexpected products or side products to be explained. En route of this investigations, known α,β-conjugated thioketones should be prepared and, if necessary, syntheses of new α,β-conjugated thioketones should be elaborated. In condensed form, the goals were:

a) Synthesis of thioketones with conjugated π-systems;

b) Conversion of these thioketones with known diazo compounds under suitable conditions into five-membered sulfur-heterocycles;

c) Analysis and identification of the resulting products and elucidation of the reaction mechanisms, which led to their formation.

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Chapter 4

1,5-Dipolar Electrocyclizations in Reactions of α-Thioxoketones and α-Thioxothioamides with Diazo Compounds[1])

Several reactions of α-thioxoketones and α-thioxothioamides with diazo compounds were investigated. Most of them proceeded *via* a reactive thiocarbonyl ylide, which underwent a [2+3] cycloaddition with the α-thioxoketone to give the '*Schönberg* products' **17**-**19** or a 1,5-dipolar electrocyclization to give the corresponding five-membered 1,3-oxathioles (**13**, **20a**, **20b**, **21**, **25**) and 1,3-dithioles (**33**, **34**, **35**), respectively. In the case of thioamide **32**, the thiocarbonyl ylides underwent a competitive 1,3-dipolar electrocyclization to yield the corresponding thiiranes. In these cases, spontaneous desulphurization led to the corresponding alkenes **36** and **37**.

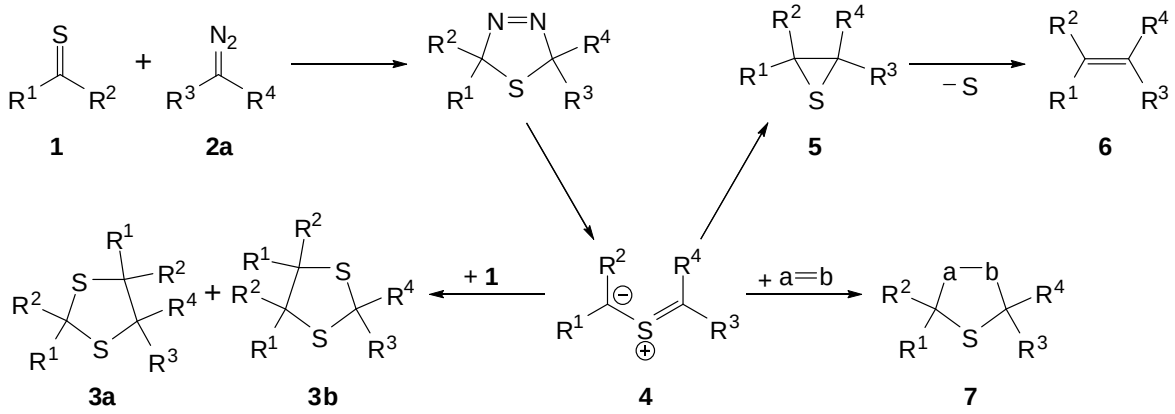
The nature of the employed thiocarbonyl or diazo compounds seems to be decisive for the reaction pathway. When the diazo compound bears at least one H-atom in the β-position to the diazo group (*i.e.* diazocyclohexane **15f**), no products of an electrocyclization could be isolated in the reactions with α-thioxoketones or α-thioxothioamides. The only products which could be isolated in these cases were 2-[(cyclohex-1-enyl)sulfanyl]-1,2-diphenyl-ethanone (**22**) and 2-[(cyclohex-1-enyl)sulfanyl]-*N*,*N*-dimethyl-2-phenylthioacetamide (**38**), which were formed by a [1,4]-H shift of the corresponding thiocarbonyl ylides.

1. Introduction. – The reactions of thiocarbonyl compounds **1** with diazo alkanes **2a** have been investigated extensively over the last few years. Most of the reactions led to 1,3-dithiolanes **3a** and **3b** by 1,3-dipolar cycloaddition of the intermediate thiocarbonyl ylide **4** with the original C=S compound (the so called *Schönberg* reaction [1] [2]) or to thiiranes **5** by 1,3-dipolar electrocyclization. The latter form alkenes **6** by S-extrusion [2-4] (*Scheme 1*). Many studies have attempted to determine the intermediates of these reactions. All results indicated the formation of thiocarbonyl ylides **4** as intermediates, which react *via* several pathways to form the products (for reviews see [5][6]). These intermediates could be intercepted by dipolarophiles to give the [2 + 3] adducts **7** in a 1,3-dipolar

[1]) D. H. Egli, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2006**, *89,* 1910.

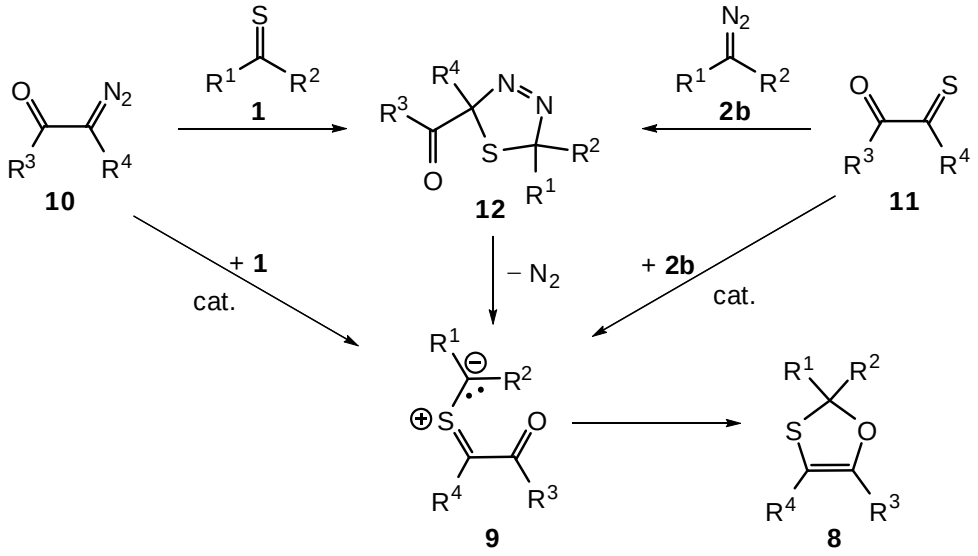
cycloaddition. This reaction led not only to the understanding of the reaction mechanism, but also opened new access to S-heterocycles.

Scheme 1



Another goal was the incorporation of the dipolarophile into the thiocarbonyl ylide, in order to promote a ring closure *via* 1,5-dipolar electrocyclization. These studies have shown that 1,3-oxathioles **8** can easily be prepared by generation of a thiocarbonyl ylide **9** *via* a $Rh_2(OAc)_4$ or $LiClO_4$ catalyzed reaction of α-diazocarbonyl compounds **10** with thiocarbonyl compounds **1,** followed by a 1,5-dipolar electrocyclization [7-9]. In a few cases, it was shown that **8** can also be prepared by the reaction of α-thioxocarbonyl compounds **11** with diazo compounds **2b** by using $Rh_2(OAc)_4$ as a catalyst [10][11]. This is not surprising, because the 5-dihydro-1,3,4-thiadiazole **12** and **9** are common intermediates in both reactions (*Scheme 2*).

Scheme 2

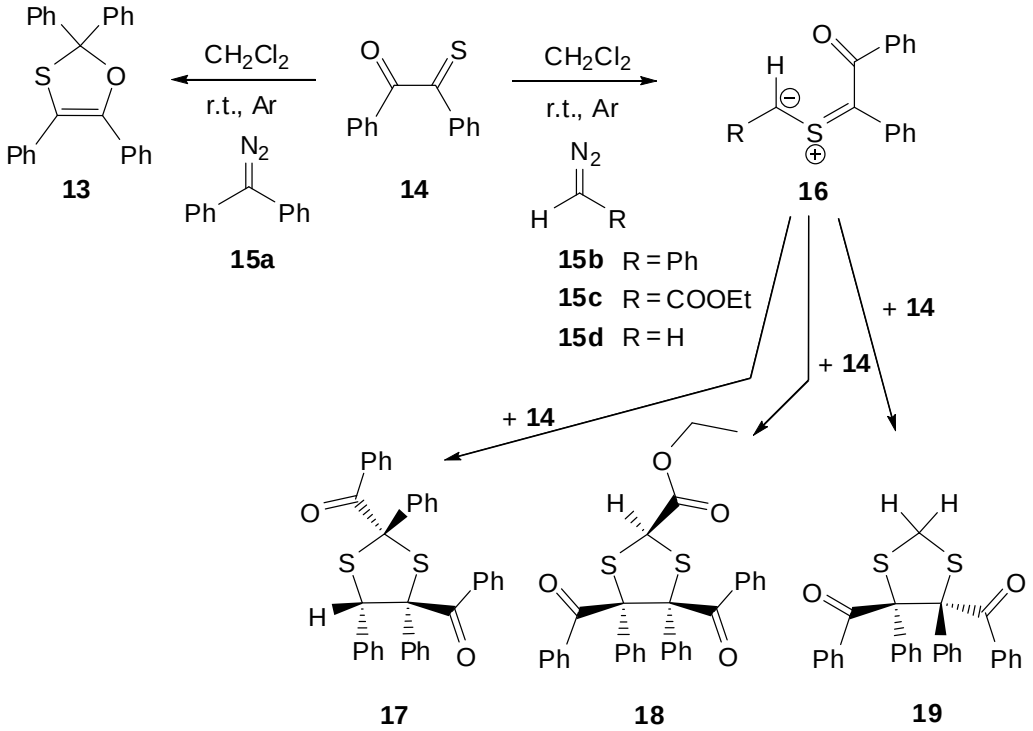


The main target of the present study was to investigate further the scope and limitations of the 1,5-dipolar electrocyclization of thiocarbonyl ylides with a conjugated π-system and, in

particular, the influence of this conjugated π-system in the thiocarbonyl compounds on the course of the reaction with diazo compounds.

2. Results and Discussion. – 2.1. *Reactions with α-Thioxocarbonyl Compounds.* As 1,2-diphenyl-2-thioxoethanone (**14**) reacted cleanly with diphenyldiazomethane (**15a**) to give 2,2,4,5-tetraphenyl-1,3-oxathiole (**13**) as the only product [11] (*Scheme 3*)[2]), **14** was selected as a suitable candidate for the reaction with phenyldiazomethane (**15b**), ethyl 2-diazoacetate (**15c**), and diazomethane (**15d**), respectively. It was expected that these reactions would lead to the corresponding 1,3-oxathioles by 1,5-dipolar electrocyclization of the intermediate thiocarbonyl ylide **16**. Unexpectedly, the products of the reaction in CH_2Cl_2 at room temperature obtained after chromatography on SiO_2 were not the expected ones. The main product in each case was yellow stinky oil, which could not be analyzed because of decomposition. The results were the same when the reaction conditions were changed (low temperature, heating, catalysis with $Rh_2(OAc)_4$ or $LiClO_4$). In each case, the corresponding racemic *Schönberg* product, *i.e.***17**-**19**, was isolated as a minor product in 15 to 25% yield (*Scheme 3*).

Scheme 3



[2]) The repetition of the reaction reported in [11] yielded **13**, which was identical with the product obtained from the reaction of 2-diazo-1,2-diphenylethanone and thiobenzophenone [7].

The structures of **17**-**19** have been established by X-ray crystallography (*Fig. 1*). The five-membered ring of **17** has a half-chair conformation twisted on S(2)-C(3). The two benzoyl groups at C(2) and C(4) are *trans* oriented, and the configuration of the Ph groups at C(2), C(4) and C(5) is *trans*, *cis*. In **18**, the ethyl group of the ester side chain is disordered over two orientations that differ slightly by a twist about this O-Et bond. Two equally occupied positions were refined for the terminal methyl groups of this moiety. The five-membered ring has an envelope conformation with C(2) as the envelope flap. The two benzoyl groups at C(4) and C(5) are *cis* to the ester group and to each other. The five-membered ring of **19** has a half-chair conformation twisted on C(1)-S(5). The benzoyl substituents lie *trans* to each other.

It is remarkable that the regioselectivity of the formation of the dithiolane ring of **17** is different to that of **18** and **19**. Furthermore, the relative configuration of the benzoyl groups at C(4) and C(5) is *cis* in **18**, but *trans* in **19**.

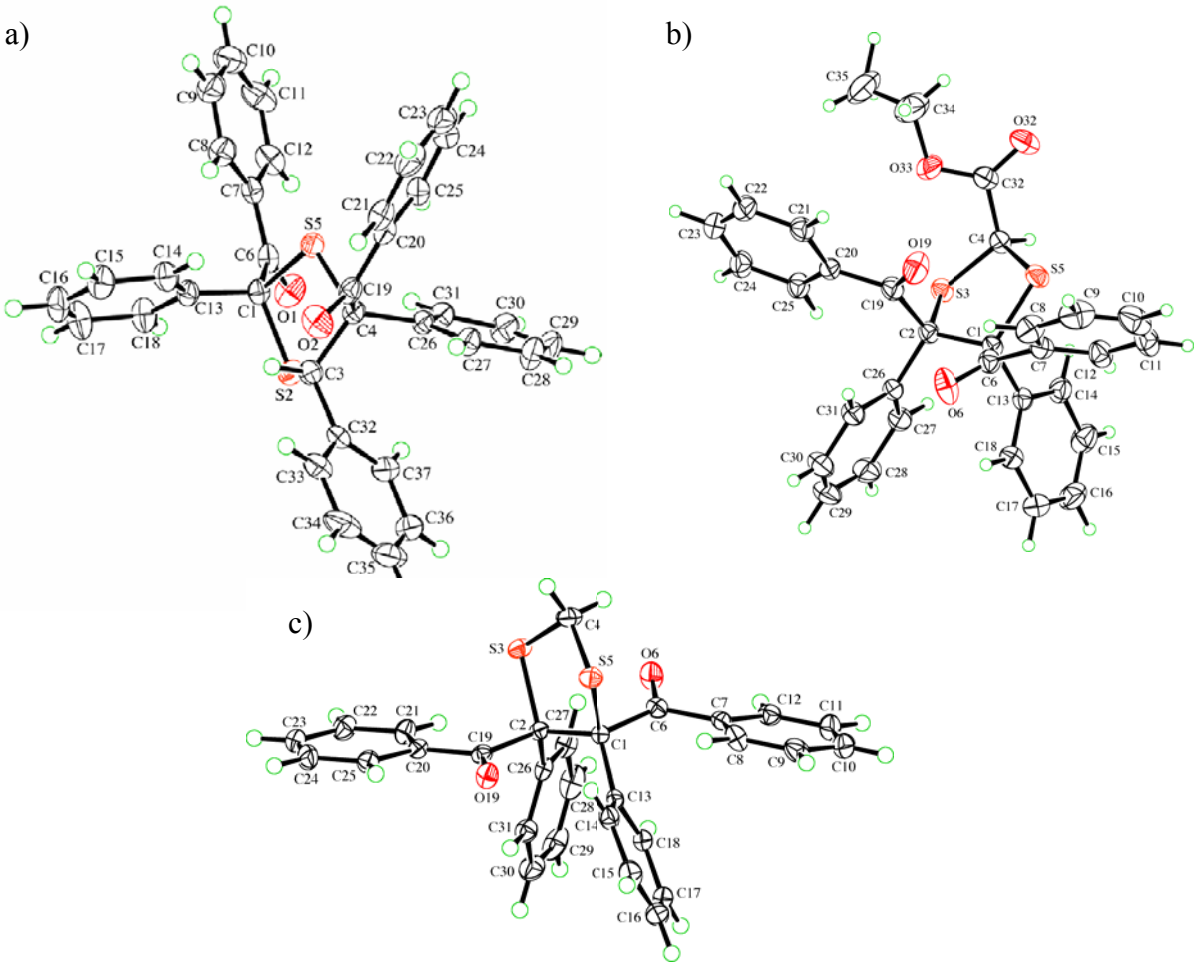
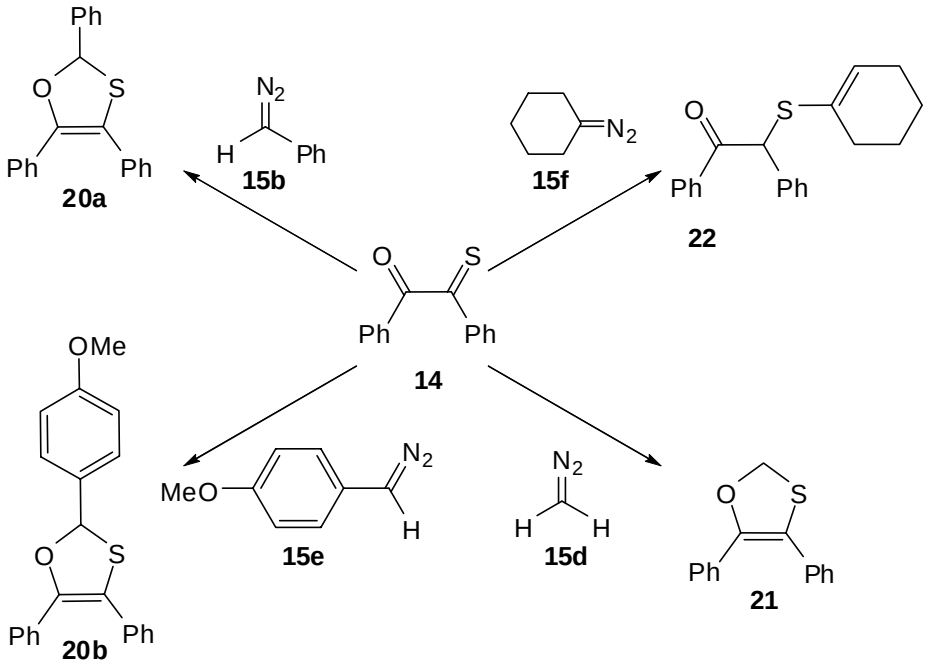


Fig. 1 *ORTEP Plots* [12] *of the molecular structure of a)* **17***, b) one of the two conformations of* **18***, and c)* **19** (50% probability ellipsoids, arbitrary numbering of the atoms)

Since the results of the reactions under various conditions did not change, we tried to isolate a product from the yellow oil by varying the purification methods. Column chromatography on silica gel (acidic) or Alox (basic) did not lead to satisfying results; therefore, 1% Et_3N was added to the eluent of the chromatography on silica gel. This procedure showed considerable advantage over all methods previously used and the best results were obtained with 3% Et_3N. By using the same reaction conditions as described above and the new conditions for the chromatographic workup, the reactions of **14** with phenyldiazomethan (**15b**), diazomethane (**15d**), and (4-methoxyphenyl)diazomethan (**15e**) gave the expected 1,3-oxathiols **20a**, **21,** and **20b** in yields of 42, 40, and 60%, respectively (*Scheme 4*). In addition to the main product, namely the 1,3-oxathiols, the corresponding alkenes, which result from a 1,3-dipolar electrocyclization of the thiocarbonyl ylide, followed by a desulphurization, were observed as by-products, and not the *Schönberg* products. These by-products were themselves reactive and led to further by-products, which were not isolated or characterized.

Scheme 4



The structure of **20b** was established by X-ray crystallography (*Fig. 2*). The five-membered ring has an envelope conformation with C(5) as the envelope flap. The planes of the Ph groups at C(2) and C(3) are twisted out of the plane defined by C(6), C(2), C(3), and C(12) by 57.6(2) and 33.1(2)°, respectively.

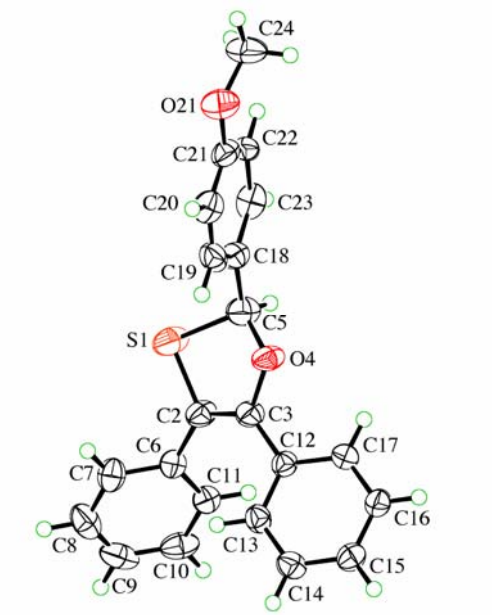
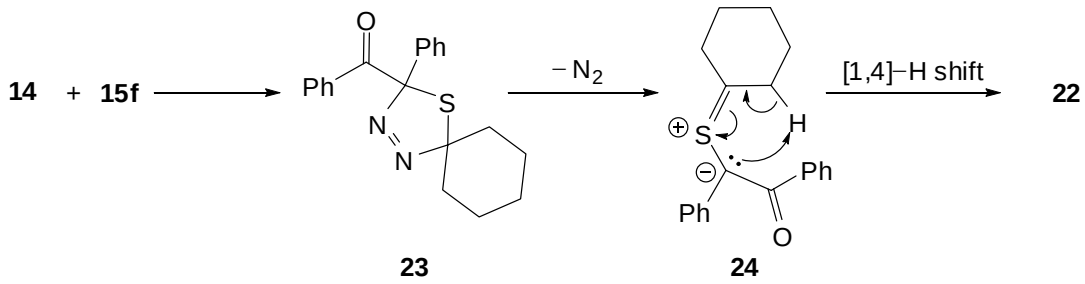


Fig. 2 *ORTEP Plot* [12] *of the molecular structure of* **20b** (50% probability ellipsoids, arbitrary numbering of the atoms)

The results described above show that the synthesis of 1,3-oxathiols *via* 1,5-dipolar electrocyclization by starting from thioketones with a conjugated keto group, is achievable with moderate to good yields. Under the chosen conditions, the 1,3-dipolar electrocyclization is a side reaction. Comparing the yields from the different experiments shows that the substituents of the diazo-component have a significant influence on the yields of the desired 1,3-oxathiols. The highest yield (81%) was observed in the already known reaction of **14** with **15a**, which lead to 1,3-oxathiol **13** [11] (*Scheme 3*).

The reaction of diazocyclohexane (**15f**) with **14** in CH_2Cl_2 at room temperature gave the sulphide **22** in 40% yield (*Scheme 5*). The structure of **22** was again established by X-ray crystallography (*Fig. 3*). The cyclohexane ring has two equally occupied disordered orientations which differ by a rotation of approximately 180° about the S-C(15) bond. The formation of **22** is easily rationalized *via* the intermediate cycloadduct **23** and the thiocarbonyl ylide **24**, which does not undergo the 1,5-dipolar electrocyclization, but a [1,4]-H shift to give 2-[(cyclohex-1-enyl)sulfanyl]-1,2-diphenylethanone (**22**) (*Scheme 5*). Similar [1,4]-H shifts in thiocarbonyl ylides are known [5][6].

Scheme 5



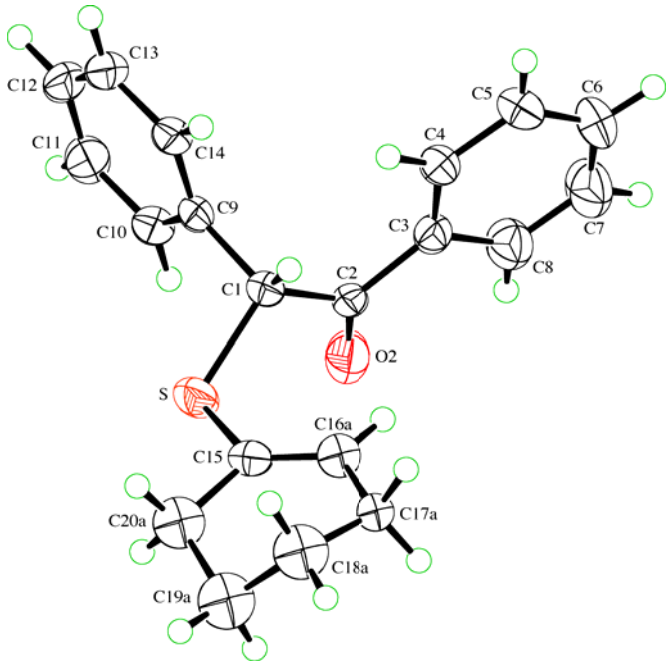
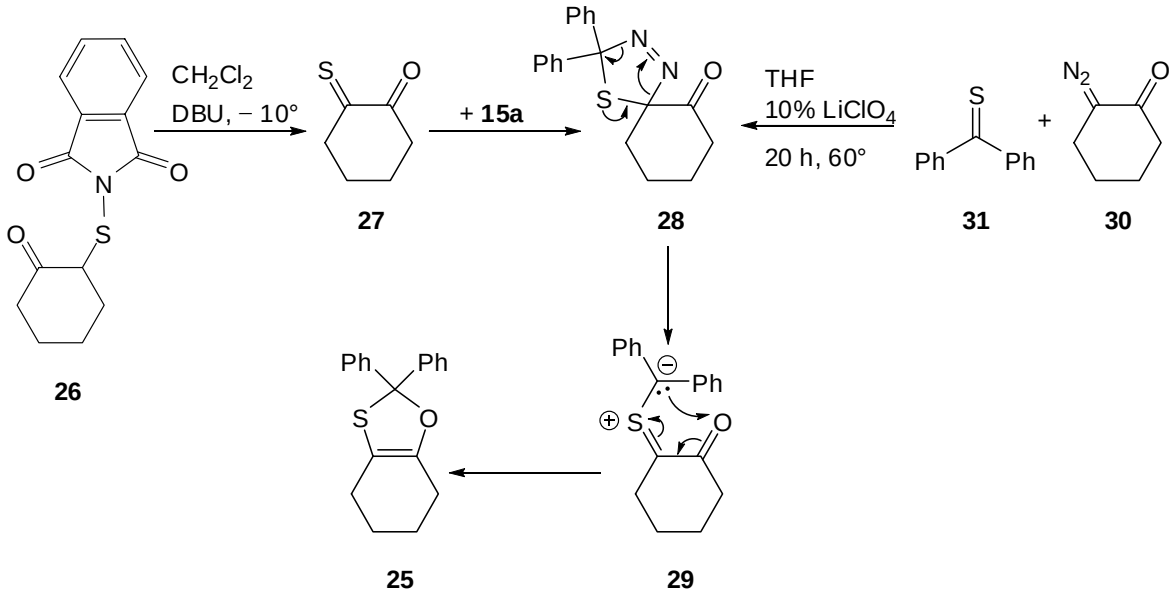


Fig. 3 *ORTEP Plot* [12] *of the molecular structure of one of the two disordered orientations of* **22** (50% probability ellipsoids, arbitrary numbering of the atoms)

The synthesis of the fused 1,3-thioxole **25** was achieved by starting from 2-[(2-oxocyclohexyl)sulfanyl]isoindole-1,3-dione (**26**) and generating the intermediate 2-thioxocyclohexanone (**27**) by DBU-catalyzed elimination of phthalimide [13][14] (*Scheme 6*). In the presence of an excess of diphenyldiazomethane (**15a**), **27** underwent a cycloaddition to yield **28,** which eliminated N_2 spontaneously to give the thiocarbonyl ylide **29**. The subsequent reaction followed the expected pathway *via* 1,5-dipolar cyclization. The same 1,3-oxathiole (**25**) has been synthesized by *Kelmendi et al.* [9]. In this case, the starting material was 2-diazocyclohexanone (**30**), which reacted with thiobenzophenone (**31**) to give the same intermediate **28**. Because of the special reaction conditions, only the reaction with diphenyldiazomethane (**15a**) was successful.

Scheme 6



The structure of **25** has been determined by X-ray crystallography (*Fig. 4*). The five-membered heterocycle has an envelope conformation with C(3) as the envelope flap, while the cyclohexene ring has a half-chair conformation twisted on C(7)-C(8).

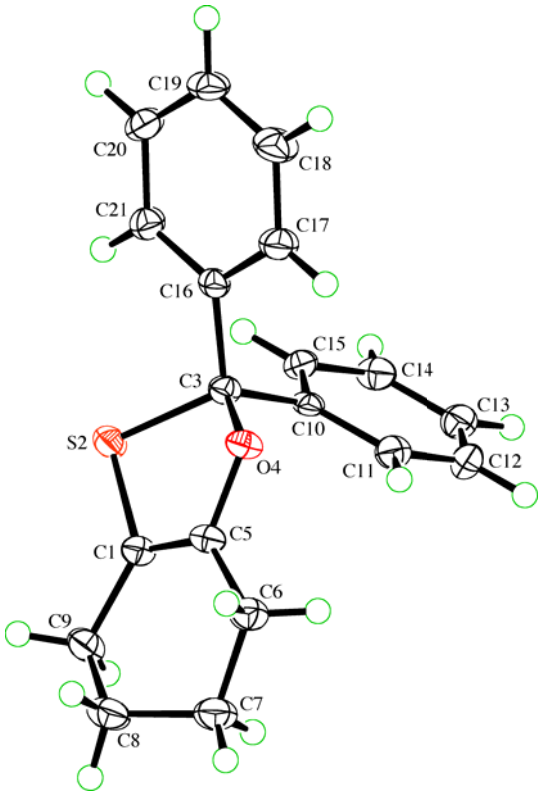
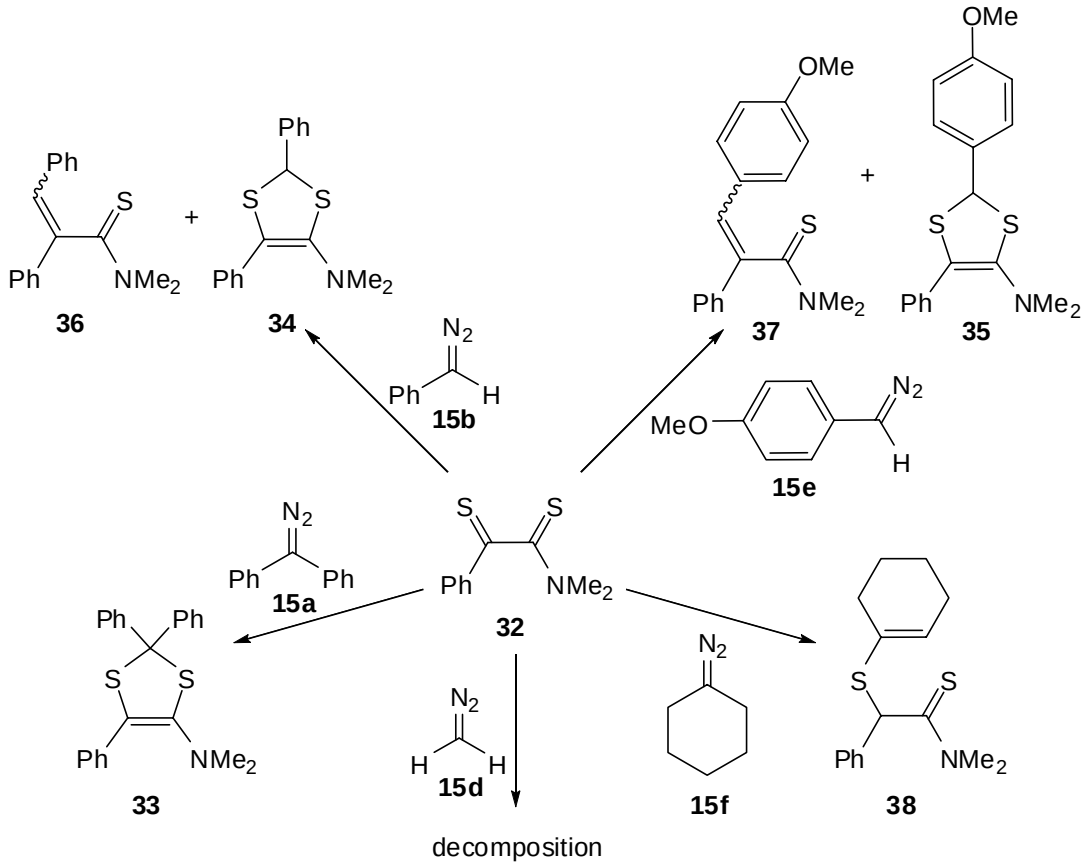


Fig. 4 *ORTEP Plot* [12] *of the molecular structure of* **25** (50% probability ellipsoids, arbitrary numbering of atoms)

2.2. Reactions with α-Thioxothioamides. After these encouraging results with α-thioxoketones, we tried to find other systems, which would react analogously. α-Thioxothioamides of type **32** are easily available and possess an unsaturated system, the thioamide group, in conjugation with the thiocarbonyl group. The reactions of **32** with diazo compounds showed that thiocarbonyl ylides are formed, which undergo a 1,5-dipolar electrocyclization to yield 1,3-dithiols (**33**-**35**) (*Scheme 7*). In all cases, the yields of the heterocyclic product were lower than with the thioxocarbonyl compound **14**. In the reactions of **32** with **15b** and **15e**, respectively, the 1,3-dipolar electrocyclization of the intermediate thiocarbonyl ylide is a more significant side reaction than in the case of **14** and yields the corresponding α,β-unsaturated thioamides **36** and **37** after desulfurization[3]). The only reaction in which no side product was formed was the one between diphenyldiazomethane (**15a**) and **32**. As in the case of α-thioxoketone **14**, the reaction of **32** with diazocyclohexane (**15f**) led to the thioenole **38** exclusively, which results from a [1,4]-H shift of the corresponding intermediate thiocarbonyl ylide. The reaction of **32** with diazomethane (**15d**) was carried out under the same conditions as those used in the case of **14**, but only decomposition was observed (TLC), and no reasonable product of a related reaction could be isolated.

[3]) These side products could not be obtained in pure form, but only as mixtures of (*E/Z*)-isomers.

Scheme 7



The structures of the 1,3-dithiole **33** and α-sulfanylthioamide **38** have been established by X-ray crystallography (*Fig. 5*).

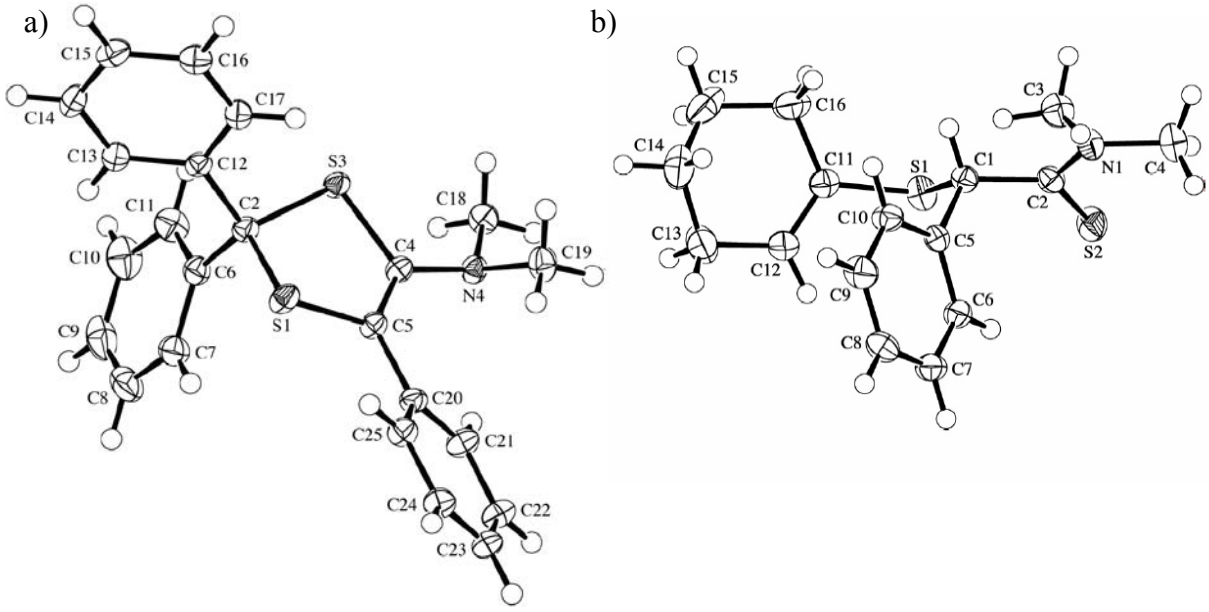


Fig. 5 *ORTEP Plot* [12] *of the molecular structure of a)* **33** *and b)* **38** (50% probability ellipsoids, arbitrary numbering of the atoms)

3. Conclusions. – We have investigated several reactions of diazo compounds with thioketones, which contain a keto or a thioamide group in the α-position. The reactions proceeded *via* thiocarbonyl ylides as intermediates, which, in most cases underwent a 1,5-dipolar electrocyclization to give the corresponding five-membered ring containing the former thiocarbonyl S-atom, *i.e.*, 1,3-oxathioles and 1,3-dithioles, respectively. In some cases, a 1,3-dipolar electrocyclization of the thiocarbonyl ylide occurred to give the corresponding thiiranes, which spontaneously desulfurized to yield the corresponding alkenes. Since 1,3-oxathioles with an H-atom in the ring are generally unstable under acidic conditions, they decomposed during chromatography on acidic or wet silica gel, and in these cases the *Schönberg* products **17**-**19** could be isolated, though in relatively low yields (10-25%).

The diazo compound used also seems to be decisive for the reaction pathway. When the diazo compound bears at least one H-atom in the β-position to the diazo group, *e.g.* diazocyclohexane (**15f**), no products of the 1,5- nor of the 1,3-dipolar electrocyclization could be isolated from the reaction with **14** or **32**. The only products isolated in these cases are products resulting from a [1,4]-H shift in the intermediate thiocarbonyl ylide. The behaviour of the α-thioxothioamide **32** under the chosen conditions is very much like that of α-thioxoketones. However, the competition of the 1,3-dipolar electrocyclization of the thiocarbonyl ylide, which produces the corresponding alkenes, is more pronounced.

We thank the analytical units of our institute for spectra and analyses, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for financial support.

Experimental Part

1. *General*. Solvents were purified prior to use by standard procedures. TLC: Aluminium sheets covered with silica gel 60 F_{254} (*Merck*); visualization by UV light or by spraying with 'mostain' soln. ($Ce(SO_4)_2$ (0.8 g), 10% H_2SO_4 (800 ml)) and heating (blue spots). Column chromatography (CC): silica gel 60 (*Merck*), 0.040 ± 0.063 mm. Medium-pressure liquid chromatography (MPLC): *Labomat VS-200* of *Labomatic* with a *HPP-VPC*-column of *Kron-Lab* (length: 540 mm, inside Ø: 40mm, max. pressure: 40 bar) was used. M.p. (not corrected): *Mettler FP 5/52*. IR Spectra: *Perkin-Elmer 1600 Series FT-IR* spectrometer; in cm^{-1}, characterization of the band intensities (transmission): 0 - 20% *vs*, 20 - 40% *s*, 40 -

60% *m*, 60 - 80% *w*. NMR Spectra: *Bruker ARX-300* (300 and 75.5 MHz, resp.); chemical shifts δ (in ppm) relative to $CDCl_3$ (7.27 resp. 77.0 ppm), coupling constants *J* in Hz; for assignments of ^{1}H-NMR signals, COSY, TOCSY and NOESY 2D- or 1D-NMR methods were applied; for assignments of ^{13}C-NMR signals, HMBC and HSQC 2D-NMR methods were employed. If not stated otherwise, the spectra were recorded in $CDCl_3$. MS: *Varian SSQ 700*; ionization by EI (70 eV) or CI (NH_3); in *m/z*, rel. intensities (%).

2. *Starting Materials.* All thiocarbonyl derivatives or precursors and the diazo compounds were prepared following known protocols: diphenyldiazomethane (**15a**) [11], phenyldiazomethane (**15b**) [15], diazomethane (**15d**) [16], diazocyclohexane (**15f**) [17], 1,2-diphenyl-2-thioxoethanone (**14**) [11], *N,N*-dimethyl-2-phenyl-2-thioxothioacetamide (**32**) [18], 2-[(2-oxocyclohexyl)sulfanyl]isoindole-1,3-dione (**26**) [13] [14]. All other reagents are commercially available.

3. *Yields*. Almost all of the diazo compounds are only stable in solution and were often used in excess. As most of the thiocarbonyl compounds were also only stable in solution, or were synthesized *in situ*, the corresponding yields were approximated. The reported yields in these cases are based on experience [11] or on the volume of N_2 evolved. If this was not possible, *i.e.* in cases of reactions lasting two or more days, yields were calculated over two or three reaction steps.

4. *General Procedure A* (*GP A*). To a soln. of thiocarbonyl compound (2-7 mmol) in CH_2Cl_2 (30-100 ml), the diazo compound (1-7 mmol) in toluene or benzene (30-130 ml) was added by means of a dropping funnel. After total conversion of the thiocarbonyl compound, monitored either by TLC, color change or evolution of N_2[4]), the solvent was evaporated and the mixture was analyzed and purified by chromatography using silica gel, which had been treated with 3% Et_3N. Furthermore, the solvent was doped with 1% of Et_3N.

General Procedure B (*GP B*). The same procedure as in *GP A* was followed, but the mixture was purified by chromatography without using Et_3N.

General Procedure C (*GP C*): To a suspension of isoindole-1,3-dione **26** (2-5 mmol) in CH_2Cl_2 (15-40 ml) at –10°, **15a** was added as a purple soln. in benzene (10-25 ml, 3-7

[4]) The evolution of N_2 was determined volumetrically using a gas burette attached to the reaction vessel.

mmol). A catalytic amount of DBU was added and the evolution of N_2 was measured volumetrically. After stirring for a few min, the solvent was removed and the mixture was analysed and purified by chromatography.

5. *Reactions of 1,2-Diphenyl-2-thioxoethanone* (**14**) *with Diazoalkanes*.

2,4-trans-*4,5*-trans-*(4-Benzoyl-2,4,5-triphenyl-1,3-dithiolane-2-yl)phenylmethanone* (**17**). According to *GP B*, **14** (3.9 mmol) in CH_2Cl_2 (60 ml) and **15b** (*ca*. 3.9 mmol) in toluene (150 ml) were used. The crude product was purified by CC (hexane/AcOEt 20:1) and recrystallized from hexane/AcOEt: 371 mg (20%) of **17**. Colorless crystals. M.p. 232-233°. IR (KBr): 3058*w*, 3028*w*, 2928*w*, 1679v*s*, 1595*s*, 1479*m*, 1489*m*, 1445*s*, 1395*w*, 1308*w*, 1228*vs*, 1184*s*, 1156*w*, 1080*w*, 1036*w*, 1018*m*, 1001*w*, 971*w*, 934*w*, 878*w*, 861*w*, 839*w*, 826*w*, 807*w*, 785*w*, 771*w*, 753*m*, 740*s*, 696v*s*, 685*s*, 658*s*, 650*s*. ^{1}H-NMR: 7.78-7.72 (*m*, 4 arom. H); 7.64-7.61 (*m*, 2 arom. H); 7.49-6.89 (*m*, 19 arom. H); 5.85 (*s*, H-C(5)). ^{13}C-NMR: 193.5, 191.5 (2*s*, 2 CO); 141.1, 135.8, 135.6, 134.1, 133.6 (5*s*, 5 arom. C); 133.3, 132.6, 130.7, 130.5, 130.1, 129.0, 128.4, 128.2, 128.0, 127.9, 127.8, 127.4, 126.6 (13*d*, 25 arom. CH); 79.5 (*s*, C(4)); 60.1 (*d*, C(5))[5]. CI-MS: 560 (100, $[M + NH_4]^+$), 543 (54, $[M + 1]^+$), 317 (67, $[M - PhCOCSPh]^+$), 285 (41), 244 (28), 214 (19). Anal. calc. for $C_{35}H_{26}O_2S_2$ (542.72): C 77.46, H 4.83, S 11.82; found: C 77.51, H 4.91, S 11.80.

Crystals suitable for an X-ray crystal-structure determination were grown from CH_2Cl_2/hexane by slow evaporation of the solvent.

Ethyl 2,4-cis-*4,5*-cis-*4,5-Dibenzoyl-4,5-diphenyl-1,3-dithiolane-2-carboxylate* (**18**). According to *GP B*, **14** (3.9 mmol) in CH_2Cl_2 (60 ml) and ethyl diazoacetate (1.02 g, 8.9 mmol; **15c**) in Et_2O (20 ml) were used. The crude product was purified by CC (hexane/AcOEt 10:1) and the product recrystallized from hexane/AcOEt: 458 mg (25%) of **18**. Colorless crystals. M.p. 195-197°. IR (KBr): 3058*w*, 3031*w*, 2984*w*, 2898*w*, 1710v*s*, 1697v*s*, 1673*vs*, 1595*m*, 1578*m*, 1490*m*, 1464*w*, 1445v*s*, 1395*w*, 1368*w*, 1221v*s*, 1182v*s*, 1160*m*, 1086*w*, 1022v*s*, 1002*w*, 971*w*, 959*w*, 933*w*, 900*w*, 872*w*, 850*w*, 806*w*, 790*w*, 766*s*, 715v*s*, 698v*s*, 660*m*, 642v*s*. ^{1}H-NMR ((D_6)-DMSO): 7.57-6.61 (*m*, 20 arom. H); 5.89 (*s*, H-C(2)); 3.78 (*qd*-like, CH_2); 0.70 (*t*, J = 7.1, Me). ^{13}C-NMR ((D_6)-DMSO): 195.1, 191.8 (2*s*, 2 CO); 167.9 (*s*, C(O)O); 139.4, 136.6, 135.7, 133.2 (4*s*, 4 arom. C); 132.3, 131.4, 130.2, 129.2, 128.2, 127.9, 127.4, 127.2, 126.8 (9*d*, 20 arom. H); 80.8, 79.4 (2*s*, C(4), C(5)); 61.6

[5]) The signal for C(2) could not be detected.

(*t*, CH_2); 47.6 (*d*, C(2)); 13.0 (*q*, Me)[6]). CI-MS: 556 (7, $[M + NH_4]^+$), 539 (9, $[M + 1]^+$), 390 (31), 389 (100). Anal. calc. for $C_{32}H_{26}O_4S_2$ (538.69): C 71.35, H 4.87, S 11.91; found: C 71.37, H 4.68, S 11.62.

Crystals suitable for an X-ray crystal-structure determination were grown from CH_2Cl_2/AcOEt by slow evaporation of the solvent.

trans-*(5-Benzoyl-4,5-diphenyl-1,3-dithiolane-4-yl)phenylmethanone* (**19**). According to *GP B*, **14** (3.9 mmol) in CH_2Cl_2 (60 ml) and **15d** (*ca.* 4-6 mmol) in Et_2O (8 ml) were used. After 10 min stirring, a small amount of AcOH was added drop-wise until the N_2-evolution ceased. The crude product was purified by CC (hexane/AcOEt 10:1): 302 mg (15%) of **19.** Colorless crystals. M.p. 189° (decomp.). IR (KBr): 3087*w*, 3061*m*, 3030*w*, 2985*w*, 2929*w*, 1681v*s*, 1594*s*, 1578*s*, 1493*s*, 1444*vs*, 1414*m*, 1317*w*, 1302*w*, 1216v*s*, 1197v*s*, 1182v*s*, 1100*m*, 1085*m*, 1035*m*, 1010v*s*, 973*w*, 937*w*, 871*w*, 842*w*, 786*w*, 769*s*, 753*w*, 742*w*, 700v*s*, 638*w*, 611v*s*. ^{1}H-NMR: 7.39-7.35 (*m*, 8 arom. H); 7.25-7.15 (*m*, 8 arom. H); 7.08-7.03 (*m*, 4 arom. H); 3.96 (*s*, CH_2). ^{13}C-NMR: 190.0 (*s*, 2 CO); 136.2, 133.3 (2*s*, 4 arom. C); 132.9, 131.0, 130.1, 128.3, 127.3, 126.9 (6*d*, 20 arom. CH); 78.5 (*s*, C(4), C(5)); 32.3 (*t*, CH_2). EI- and CI-MS: no measurement possible. Anal. calc. for $C_{29}H_{22}O_2S_2$ (466.63): C 74.65, H 4.75, S 13.74; found: C 74.90, H 4.61, S 13.45.

Crystals suitable for an X-ray crystal-structure determination were grown from AcOEt by slow evaporation of the solvent.

4,5-Diphenyl-1,3-oxathiole (**21**). According to *GP A*, **14** (*ca.* 4 mmol) in CH_2Cl_2 (83 ml) and **15d** (*ca*. 5 mmol) in Et_2O (*ca.* 50 ml) were used. The crude product was purified by CC (hexane/AcOEt 4:1 + 3% Et_3N) and recrystallized from hexane/Et_2O: 368 mg (*ca.* 40%) of **21**. Yellowish crystals. M.p. 41-43°. IR (Golden Gate, ATR): 3057*w*, 3032*w*, 2915*w*, 2856*w*, 1691*w*, 1616*m*, 1593*m*, 1571*m*, 1494*m*, 1443*m,* 1329*m*, 1313*w*, 1297*w*, 1208*m*, 1072*w*, 1058*s*, 1028*m*, 1000*m*, 988*m*, 942*s*, 924*m*, 847*m*, 771*m*, 755v*s*, 742*s*, 693v*s*, 675*s*. ^{1}H-NMR: 7.36-7.18 (*m*, 10 arom. H); 5.69 (*s*, $H_2C(2)$). ^{13}C-NMR: 143.9 (*s*, C(5)); 132.4, 130.4 (2*s*, 2 arom. C); 129.0, 128.5, 128.2, 128.0, 127.7, 127.4 (6*d*, 10 arom. CH); 111.4 (*s*, C(4)); 72.7 (*t*, $H_2C(2)$). CI-MS (NH_3): 242 (17), 241 (100, $[M + 1]^+$).

[6]) Because of the doubling of some signals, the compound is either a mixture of isomers or conformers.

2,4,5-Triphenyl-1,3-oxathiole (**20a**). According to *GP A*, **14** (*ca.* 2.4 mmol) in CH_2Cl_2 (30 ml) and **15b** (*ca*. 3 mmol) in toluene (100 ml) were used. The crude product was purified by CC (hexane/AcOEt 5:1 + 3% Et_3N) and recrystallized from hexane/CH_2Cl_2: 317 mg (*ca.* 45%) of **20a**. Yellowish crystals. M.p. 74-75°. IR (Golden Gate, ATR): 3058*w*, 3034*w*, 2887*w*, 2868*w*, 1620*w*, 1598*w*, 1573*w*, 1494*w*, 1453*w*, 1444*w*, 1318*w*, 1248*m*, 1215*w*, 1056*m*, 1024*w*, 990*m*, 954*m*, 916*w*, 877*w*, 827*w*, 780*w*, 752*s*, 715*m*, 692*s,* 684*s*. ^{1}H-NMR: 7.66-7.21 (*d*-like, 2 arom. H); 7.44-7.17 (*m*, 13 arom. H); 7.04 (*s*, HC(2)). ^{13}C-NMR: 142.6 (*s*, C(5)); 139.6, 132.5, 130.6 (3*s*, 3 arom. C); 129.2, 129.1, 128.7, 128.3, 128.2, 127.8, 127.6, 126.4 (8*d*, 15 arom. CH); 111.3 (*s*, C(4)); 87.3 (*d*, HC(2)). CI-MS (NH_3): 318 (22), 317 (100, $[M + 1]^+$). Anal. calc. for $C_{21}H_{16}OS$: C 79.71, H 5.10, S 10.13; found: C 79.62, H 4.95, S 10.17.

2-(4-Methoxyphenyl)-4,5-diphenyl-1,3-oxathiole (**20b**). According to *GP A*, **14** (*ca.* 2 mmol) in CH_2Cl_2 (30 ml) and **15e** (*ca*. 3 mmol) in benzene (20 ml) were used. The crude product was purified by CC (hexane/AcOEt 30:1 + 1% Et_3N) and recrystallized from hexane/CH_2Cl_2: 410 mg (40-55%) of **20b**. Yellowish crystals. M.p. 104-108°. IR (Golden Gate, ATR): 3056*w*, 3007*w*, 2956*w*, 2928*w,* 2906*w*, 2869*w*, 2834*w*, 1686*w*, 1625*w*,1609*m*, 1585*w*, 1511*s*, 1494*m*, 1464*w*, 1443*m*, 1356*w*, 1317*w*, 1305*m*, 1289*w*, 1243v*s*, 1218*m*, 1171*s*, 1107*w*, 1082*w*, 1056*s*, 1026*s*, 984*m*, 956*m*, 915*w*, 881*w*, 833*s*, 777*m*, 763*m*, 754*s*, 697*s*, 683*s*. ^{1}H-NMR: 7.63-7.58 (*d*-like, 2 arom. H); 7.39-7.18 (*m*, 10 arom. H); 7.01 (*s*, HC(2)); 6.96-6.91 (*d*-like, 2 arom. H); 3.82 (*s*, MeO). ^{13}C-NMR: 160.4 (*s*, 1 arom. C); 143.0 (*s*, C(5)); 132.6, 131.4, 130.7 (3*s*, 3 arom. C); 129.1, 128.6, 128.2, 128.1, 127.7, 127.6 (6*d*, 12 arom. CH); 114.0 (*d*, 2 arom. CH); 111.8 (*s*, C(4)); 87.4 (*d*, C(2)); 55.4 (*q*, MeO). CI-MS (NH_3): 348 (24), 347 (100, $[M + 1]^+$), 315 (39, $[M - MeO]^+$). ESI-MS: 369 (100, $[M + Na]^+$).

Crystals suitable for an X-ray crystal-structure determination were grown from hexane/AcOEt by slow evaporation of the solvent.

2-[(Cyclohexen-1-yl)sulfanyl]-1,2-diphenylethanone (**22**). According to *GP B*, a soln. of **15f** (*ca.* 7 mmol) in CH_2Cl_2 (40 ml) was added drop-wise to a soln. of **14** (*ca.* 6.4 mmol) in CH_2Cl_2 (100 ml). Purification of the crude product by MPLC (hexane/AcOEt 20:1) afforded 790 mg (40%) of **22**. Yellowish crystals. M.p. 61-63°. IR (KBr): 3062*w*, 3027*w*, 2936v*s*, 2909*s*, 2859*s*, 2834*m*, 1672v*s*, 1596*s*, 1580*s*, 1493*m*, 1451v*s*, 1433*m*, 1342*m*, 1322*m*, 1307*m*, 1296*m*, 1274*s*, 1212*m*, 1191*s*, 1169*s*, 1136*m*, 1075*m*, 1054*w*, 1007*s*, 999*s*,

929*w*, 914*m*, 868*w*, 844*w*, 831*w*, 797*w*, 782*w*, 758*s*, 723*s*, 694v*s*, 681*s*, 640*s*. ^{1}H-NMR ((D$_6$)-DMSO): 8.09-8.06 (*m*, 2 arom. H); 7.64-7.59 (*m*, 1 arom. H); 7.52-7.47 (*m*, 4 arom. H); 7.35-7.24 (*m*, 3 arom. H); 6.22 (*s*, H-C(2)); 5.70-5.68 (*m*, =CH)[7]); 1.94-1.40 (*m*, 4 CH$_2$). ^{13}C-NMR ((D$_6$)-DMSO): 195.0 (*s*, CO); 136.8, 135.3 (2*s*, 2 arom. C); 130.6 (*s*, =C-S); 133.5 (*d*, C(2)); 129.3, 128.7, 128.4, 127.6 (4*d*, 10 arom. CH); 54.1 (*d*, =CH); 30.1, 25.9, 22.8, 21.1 (4*t*, 4 CH$_2$). CI-MS: 310 (23), 309 (100, [*M* + 1]$^+$), 214 (32). Anal. calc. for C$_{20}$H$_{20}$OS (308.44): C 77.88, H 6.54, S 10.40; found: C 77.69, H 6.37, S 10.10.

Crystals suitable for an X-ray crystal-structure determination were grown from hexane/AcOEt by slow evaporation of the solvent.

6. *Reaction of 2-Thioxocyclohexanone* (**37**) *with Diphenyldiazomethane* (**15a**).

2,2-Diphenyl-4,5,6,7-tetrahydrobenzo-1,3-oxathiole (**25**). According to *GP C,* a suspension of 2-[(2-oxocyclohexyl)sulfanyl]isoindole-1,3-dione (**26**; 1.0 g, 3.6 mmol) [13][14] was treated with a catalytic amount of DBU and an excess of **15a** in Et$_2$O. CC (hexane/AcOEt 15:1) yielded 702 mg (51%) of **25**. Pale-bluish crystals. M.p. 107-109°. IR (KBr): 3080*w*, 3059*w*, 3019*w*, 3001*w*, 2950*s*, 2917*s*, 2884*m*, 2855*m*, 2841*s*, 1682*s*, 1598*w*, 1585*w*, 1488*s*, 1445v*s*, 1388*w*, 1353*w*, 1340*m*, 1313*w*, 1289*w*, 1261*w*, 1225*m*, 1206*s*, 1176v*s*, 1145v*s*, 1133*s*, 1109*w*, 1071*m*, 1028*s*, 997*m*, 986v*s*, 958*s*, 933*w*, 916*m*, 900*m*, 882*s*, 857*w*, 836*w*, 819*w*, 763v*s*, 754v*s*, 696v*s*. ^{1}H-NMR : 7.54-7.50 (*m*, 4 arom. H); 7.34-7.23 (*m*, 6 arom. H); 2.29-2.24 (*m*, 2 H); 2.17-2.12 (*m*, 2 H); 1.73-1.65 (*m*, 4 H). ^{13}C-NMR: 144.7 (*s*, 2 arom. C); 143.1 (*s*, C(7a)); 128.0, 127.9, 126.4 (3*d*, 10 arom. CH); 104.5, 100.7 (2*s*, C(2), C(3a)); 24.2, 23.5, 23.0, 22.4 (4*t*, 4 CH$_2$). EI-MS: 294 (26, $M^{+\cdot}$), 266 (11), 262 (23), 261 (100), 237 (28), 223 (13), 187 (15), 167 (18), 166 (10), 165 (49), 105 (21, [PhCO]$^+$), 77 (14, Ph$^+$). Anal. calc. for C$_{19}$H$_{18}$OS (294.42): C 77.51, H 6.16; found: C 77.49, H 6.08.

Crystals suitable for an X-ray crystal-structure determination were grown from hexane by slow evaporation of the solvent.

7. *Reactions of* N,N-*Dimethyl-2-phenyl-2-thioxothioacetamide* (**32**) *with Diazoalkanes.*

N,N-*Dimethyl*-N-*(2,2,5-triphenyl-1,3-dithiol-4-yl)amine* (**33**). According to *GP A,* a soln. of **32** (200 mg, 1.1 mmol) in CH$_2$Cl$_2$ (20 ml) and **15a** (*ca*. 1.5 mmol) in benzene (15 ml) were used. The crude product was purified by CC (hexane/AcOEt 10:1 to 4:1): 170 mg (*ca.* 43%) of **33**. Yellowish crystals. M.p. 122-125°. IR: 3053*w*, 3013 *m*, 2986 *m*, 2950 *m*, 2923 *m*, 2897 *m*, 2862 *m*, 2834 *m*, 2792 *m*, 1659 *w*, 1590 *m*, 1570 *s*, 1553 *vs*, 1483 *vs*, 1452

[7]) When the spectrum was recorded in CDCl$_3$, the signals of HC(2) and =CH overlapped.

s, 1440 *vs*, 1406 *m*, 1311 *s*, 1210 *m*, 1071 *s*, 1045 *s*, 1033 *s*, 998 *m*, 961 *m*, 902 *m*, 861 *s*, 833 *m*, 800 *w*, 756 *vs*, 737 *vs*, 698 *vs*, 690 *vs*, 658 *s*, 629 *m*, 618 *m*, 608 *m*. ^{1}H-NMR: 7.62-7.54 (*d*-like, 4 arom. CH); 7.43-7.37 (*d*-like, 2 arom. CH); 7.25-7.05 (*m*, 9 arom. CH); 2.42 (*s*, Me_2N). ^{13}C-NMR: 143.7 (*s*, 2 arom. C); 142.7 (*s*, arom. C); 134.5 (*s*, C(4)); 129.2, 128.3, 128.0, 127.9, 127.8, 127.4, 126.7 (7*d*, 15 arom. C); 117.6 (*s*, C(5)); 70.5 (*s*, C(2)); 44.2 (*q*, Me_2N). CI-MS (NH_3): 378 (12), 377 (28), 376 (100, $[M + 1]^+$), 344 (24, $[M$-S + $1]^+$), 199 (17), 180 (15).

Crystals suitable for an X-ray crystal-structure determination were grown from hexane/CH_2Cl_2 by slow evaporation of the solvent.

N-*(2,5-Diphenyl-1,3-dithiol-4-yl)*-N,N-*dimethylamine* (**34**). According to *GP A,* a suspension of **32** (250 mg, 1.2 mmol) in toluene (20 ml) and **15b** (*ca*. 15 mmol) in toluene (100 ml) were used. The mixture was separated by CC (hexane/AcOEt 10:1 + 1% Et_3N): 90 mg (*ca.* 25%) of **34** and 80 mg (ca. 25%) of a mixture of (*E*)- and (*Z*)-N,N-*Dimethyl-2,3-diphenylthioacrylamide* (**36**). Data of **34**: Yellowish oil. IR (KBr): 3059*m*, 3026*m*, 2932*m*, 2863*m*, 2788*w*, 1679*s*, 1647v*s* (enamin), 1597*s*, 1580*s*, 1554*m*, 1514*s*, 1493v*s*, 1451v*s*, 1392v*s*, 1333*w*, 1273*s*, 1206*m*, 1176*m*, 1142*s*, 1073*s*, 1030*m*, 1001*w*, 993*w*, 963*w*, 939*w*, 905*w*, 886*w*, 860*w*, 837*w*, 808*w*, 782*w*, 755*s*, 726*s*, 697v*s*. ^{1}H-NMR: 7.62-7.51 (*m*, 4 arom. H); 7.36-7.18 (*m*, 6 arom. H); 5.78 (*s*, HC(2)); 2.59 (*s*, Me_2N). ^{13}C-NMR: 141.4 (*s*, C(4)); 141.1, 134.1 (2*s*, 2 arom. C); 128.6, 128.2, 128.0, 126.9, 126.7 (5*d*, 10 arom. CH); 115.1 (*s*, C(5)); 50.0 (*d*, C(2)); 44.2 (*q*, Me_2N). CI-MS (NH_3): 301 (21), 300 (100, $[M + 1]^+$).

Data of **36**: IR (KBr): 3078*m*, 3054*m*, 3022*m*, 2929*s*, 2857*m*, 1598*m*, 1574*w*, 1513v*s*, 1494v*s*, 1446v*s*, 1391v*s*, 1318*w*, 1269v*s* ($CSNMe_2$), 1203*w*, 1181*m*, 1146v*s*, 1116v*s*, 1076*s*, 1049*m*, 1030*m*, 1000*w*, 949*m*, 922*m*, 886*m*, 870*w*, 796*w*, 765v*s*, 714v*s,* 695v*s*. ^{1}H-NMR: 7.57-7.06 (*m*, 10 arom. H); 6.73, 6.69 (2*s* (1:3.5), =CH); 3.56, 3.49, 3.28, 3.12 (4*s* (1:3:3:1), Me_2N). ^{13}C-NMR (only the signals of the main isomer are given): 201.7 (*s*, CS); 143.4 (*s*, C(2)); 135.8, 135.5 (2*s*, 2 arom. C); 129.3, 128.7, 128.6, 128.5, 128.1, 127.8, 127.4 (7*d*, 10 arom. CH, =CH); 43.1, 42.9 (2*q*, Me_2N). CI-MS (NH_3): 269 (19), 268 (100, $[M + 1]^+$).

N-*[2-(4-Methoxyphenyl)-5-phenyl-1,3-dithiol-4-yl]*-N,N-*dimethylamine* (**35**). According to *GP A,* a suspension of **32** (280 mg, 1.34 mmol) in toluene (20 ml) and **15e** (*ca*. 2 mmol) in benzene (20 ml) were used. The mixture was separated by CC (hexane/AcOEt 10:1 + 1%

Et_3N): 80 mg (*ca.* 20%) of **35**, and 52 mg (*ca.* 13%) of (E/Z)-*3-(4-Methoxyphenyl)*-N,N-*dimethyl-2-phenylthioacrylamide* (**37**). Data of **35**: Yellowish oil. IR (Golden Gate, ATR): 3058*w*, 3026*w*, 2931*w*, 2362*w*, 1678*w*, 1645*m*, 1596*w*, 1579*w*, 1551*w*, 1492*w*, 1449*m*, 1393*w*, 1314*w*, 1266*w*, 1244*w*, 1206*w*, 1175*w*, 1144*w*, 1103*w*, 1073*w*, 1028*w*, 993*w*, 904*w*, 846*w*, 755*w*, 725*m*, 694*s*. ^{1}H-NMR: 7.55-7.51 (*m*, 4 arom. H); 7.32-7.18 (*m*, 3 arom. H); 6.88-6.83 (*m*, 2 arom. H); 5.80 (*s*, HC(2)); 3.79 (*s*, MeO); 2.59 (*s*, Me_2N). ^{13}C-NMR: 159.6 (*s*, arom. C); 141.4 (*s*, C(4)); 134.1, 133.0, 129.9 (3*s*, 3 arom. C); 128.2, 128.2, 128.0, 126.6 (4*d*, 7 arom. CH); 113.9 (*d*, 2 arom. CH); 55.2 (*q*, MeO); 49.9 (*d*, HC(2)); 44.2 (*q*, Me_2N). CI-MS (NH_3): 331 (21), 330 (100, $[M + 1]^+$).

Data of **37**[8]): ^{1}H-NMR: 8.60 (*s*, =CH); 7.79-7.76 (*d*-like, arom. H); 7.54-7.51 (*d*-like, arom. H); 7.46-7.25 (*m*, arom. H); 7.03-6.81 (*m*, arom. H); 6.69-6.64 (*s*, =CH); 3.81, 3.74 (2*s* (1:4), MeO); 3.57, 3.48, 3.27, 3.13 (4*s* (1:3:3:1), Me_2N). ^{13}C-NMR: 202.1 (*s*, CS); 159.0 (*s*, arom. C); 141.6, 136.2 (2*s*, 2 arom. C); 130.7, 129.3, 128.6, 127.9 (4*d*, 7 arom. CH); 113.4 (*d*, 2 arom. CH); 55.2 (*s*, MeO); 43.2, 43.0 (2*q*, Me_2N). CI-MS (NH_3): 299 (21), 298 (100, $[M + 1]^+$), 269 (14, $[M\text{-}Me_2NH + NH_3]^+$).

2-[(Cyclohexen-1-yl)sulfanyl]-N,N-*dimethyl-2-phenylethanethioamide* (**38**). According to *GP A,* a soln. of **32** (313 mg, 1.5 mmol) in CH_2Cl_2 (25 ml) and **15f** (*ca.* 2 mmol) in CH_2Cl_2 (15 ml) were used. The crude product was purified by CC (hexane/AcOEt 10:1 to 4:1): 240 mg (*ca.* 55%) of **38**. Yellowish crystals. M.p. 110-111°. IR: 3079*w*, 3053*w*, 3024*m*, 3002*w*, 2940*vs*, 2918*vs*, 2851*s*, 2826*s*, 2657*w*, 1636*w*, 1600*w*, 1511*vs*, 1493*vs*, 1452*s*, 1435*s*, 1413*s*, 1385*vs*, 1339*m*, 1267*vs*, 1237*s*, 1182*m*, 1133*vs*, 1110*vs*, 1072*m*, 1051*m*, 1036*m*, 911*w*, 901*w*, 846*w*, 830*w*, 796*m*, 752*m*, 728*vs*, 698*s*, 640*w*. ^{1}H-NMR: 7.55-7.52 (*d*-like, 2 arom. H); 7.35-7.23 (*m*, 3 arom. H); 5.86-5.83 (*m*, =CH); 5.5.9 (*s*, HC(2)); 3.47, 3.22 (2*s*, Me_2N) 2.22-2.00 (*m*, 4 H, cyclohexenyl); 1.69-1.49 (*m*, 4 H, cyclohexenyl). ^{13}C-NMR: 199.8 (*s*, C=S); 137.8 (*s*, arom. C); 132.0 (*d*, arom. C); 131.8 (s, =C-S); 128.3, 127.7, 127.6 (3*d*, 4 arom. C); 60.3 (*d*, C(2)); 45.3, 42.4 (*q*, Me_2N); 30.8, 26.6, 23.3, 21.5 (4*t*, 4 CH_2). EI-MS: 291 (9, $M^{+\cdot}$), 259 (40, $[M\text{-}S]^+$), 216 (20, $[M\text{-}S\text{-}Me_2N]^+$), 182 (22), 178 (52, [*M*-S-cyclohexenyl]$^+$) 146 (100, [*M*-2S-cyclohexenyl]$^+$), 131 (39), 116 (19).

Crystals suitable for an X-ray crystal-structure determination were grown from hexane/CH_2Cl_2, by slow evaporation of the solvent.

[8]) Some signals of the NMR-spectra indicate the presence of (*E/Z*)-isomers of **37**. In the ^{13}C-NMR spectrum, only signals of the main isomer are given.

8. *X-Ray Crystal-Structure Determination of* **17**, **18**, **19**, **20b**, **22**, **25**, **33**, and **38** (*Tables 1* and *2* and *Figs. 1-5*)[9]). In the case of **17**, all measurements were made on a *Rigaku AFC5R* diffractometer using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and a 12 kW rotating anode generator. In all other cases, all measurements were performed on a *Nonius KappaCCD* diffractometer [19] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream* 700 cooler. The data collection and refinement parameters are given in *Tables 1* and *2*, and views of the molecules are shown in *Figs. 1-5*. For **17**, the intensities were corrected for *Lorentz* and polarization effects, but not for absorption. Equivalent reflections were merged. For all other structures, data reduction was performed with *HKL Denzo* and *Scalepack* [20]. The intensities were corrected for *Lorentz* and polarization effects, and with the exception of **18**, an absorption correction based on the multi-scan method [21] was applied. Equivalent reflections were merged, except for the *Friedel* pairs in **20b** and **33**. The structures were solved by direct methods using SHELXS97 [22] (**17**, **18**) and SIR92 [23] (**19**, **20b**, **22**, **25**, **33**, **38**), which revealed the positions of all non-H-atoms. In the case of **18**, the terminal Me group of the ethyl ester side chain is disordered and two equally occupied positions were refined for this group. The cyclohexene ring of **22** is also disordered and the two conformations differ by a rotation of approximately 180° about the S-C(15) bond. Two positions with equal site occupation factors were defined for each unsubstituted C-atom in the ring. However, some poor C,C bond lengths and elongated atomic displacement ellipsoids when these atoms were refined anisotropically suggest that the model does not fully describe the disorder and that the ring may adopt several conformations. The non-H-atoms were refined anisotropically in all structures, except for the disordered atoms of **22**, which were refined only isotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for the methyl groups in **20b**, **33** and **38**). The refinement of the structures **17**, **18**, **19**, **20b**, **22**, and **25** was carried out on *F* using full-matrix least-squares procedures, which minimized the function $\Sigma w(|F_o| - |F_c|)^2$. The refinement of **33** and **38** was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in the cases of **18** and **20b**. Compound **33** is achiral,

[9]) CCDC-608137–608144 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Center via* http://www.ccdc.cam.ac.uk/data_request/cif.

but crystallized in a non-centrosymmetric space group. Refinement of the absolute structure parameter [24] yielded a value of 0.00(5), which confidently confirms that the refined coordinates represent the true absolute structure. The absolute structure parameter for **20b** refined to 0.35(15), which is insufficiently precise to be able to deduce any information about the absolute configuration of the molecule. The presence of an inversion twin cannot be excluded. According to the preparation of the material, it has to be racemic. Neutral atom scattering factors for non-H-atoms were taken from [25a], and the scattering factors for H-atoms were taken from [26]. Anomalous dispersion effects were included in F_c [27]; the values for f' and f'' were those of [25b]. The values of the mass attenuation coefficients are those of [25c]. All calculations were performed using the teXsan [28] (**17**, **18**, **19**, **22**, and **25**) or the SHELXL97 [29] program (**20b**, **33,** and **38**).

Table 1. *Crystallographic Data of Compounds* **17**, **18**, **19**, **22**, and **25**

	17	**18**
Crystallized from	CH_2Cl_2/hexane	CH_2Cl_2/AcOEt
Empirical formula	$C_{35}H_{26}O_2S_2$	$C_{32}H_{26}O_4S_2$
Formula weight [g mol^{-1}]	542.71	538.67
Crystal color, habit	colorless, tablet	colorless, prism
Crystal dimensions [mm]	0.18 × 0.30 × 0.43	0.22 × 0.30 × 0.30
Temperature [K]	173(1)	298(1)
Crystal system	monoclinic	triclinic
Space group	$P2/c$	$P\bar{1}$
Z	4	2
Reflections for cell determination	25	6604
2θ range for cell determination [°]	21–37	5–74
Unit cell parameters a [Å]	19.819(3)	10.2453(2)
b [Å]	9.031(4)	10.4024(1)
c [Å]	16.328(3)	13.8478(2)
α [°]	90	100.2566 (6)
β [°]	106.39(1)	98.8651(6)
γ [°]	90	106.5469 (6)
V [Å^3]	2804(1)	1358.90(4)
D_x [g cm^{-3}]	1.285	1.316
μ(MoK_α) [mm^{-1}]	0.221	0.232
Scan type	$\omega/2\theta$	ω
2θ(max) [°]	55	55
Transmission factors (min; max)	-	-
Total reflections measured	7085	22427
Symmetry independent reflections	6447	6226
Reflections used $[I > 2\sigma(I)]$	4411	4633
Parameters refined	352	353
Final R	0.0661	0.0494
wR	0.0691	0.0558
Weights: p in $w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$	0.005	0.01
Goodness of fit	2.401	2.162
Final Δ_{max}/σ	0.0003	0.02
$\Delta\rho$ (max; min) [e Å^{-3}]	0.71; -0.41	0.37; -0.26

Table 1. *(continued)*

	19	**22**	**25**
Crystallized from	AcOEt	hexane/AcOEt	hexane
Empirical formula	$C_{29}H_{22}O_2S_2$	$C_{20}H_{20}OS$	$C_{19}H_{18}OS$
Formula weight [g mol^{-1}]	466.61	308.44	294.41
Crystal color, habit	colorless, prism	pale-yellow, prism	colorless, prism
Crystal dimensions [mm]	0.15 × 0.15 × 0.20	0.12 × 0.18 × 0.27	0.20 × 0.22 × 0.25
Temperature [K]	160(1)	160(1)	160(1)
Crystal system	monoclinic	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/c$	$P2_1/n$
Z	4	4	4
Reflections for cell determination	43672	34702	25782
2θ range for cell determination [°]	2–60	2–55	4–60
Unit cell parameters a [Å]	14.3898(1)	9.6064(2)	8.5780(1)
b [Å]	9.5516(1)	10.4524(2)	12.5949(2)
c [Å]	17.1675(2)	16.5859(3)	13.9084(2)
α [°]	90	90	90
β [°]	105.2059(4)	101.7945(7)	96.2541(7)
γ [°]	90	90	90
V [Å^3]	2276.99(4)	1630.23(5)	1493.71(4)
D_x [g cm^{-3}]	1.361	1.257	1.309
μ(MoK_α) [mm^{-1}]	0.259	0.198	0.213
Scan type	ϕ and ω	ϕ and ω	ϕ and ω
$2\theta_{(max)}$ [°]	60	55	60
Transmission factors (min; max)	0.825; 0.964	0.861; 0.978	0.897; 0.959
Total reflections measured	59019	36152	39877
Symmetry independent reflections	6668	3734	4358
Reflections used $[I > 2\sigma(I)]$	5450	2871	3384
Parameters refined	298	194	190
Final R	0.0398	0.0784	0.0433
wR	0.0466	0.0832	0.0414
Weights: p in $w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$	0.01	0.007	0.005
Goodness of fit	2.302	4.726	2.484
Final Δ_{max}/σ	0.001	0.0003	0.0004
$\Delta\rho$ (max; min) [e Å^{-3}]	0.38; -0.25	0.85; -0.47	0.31; -0.27

Table 2. Crystallographic Data of Compounds **20b**, **33**, and **38**

	20b	**33**	**38**
Crystallized from	hexane/AcOEt	hexane/CH_2Cl_2	hexane/CH_2Cl_2
Empirical formula	$C_{22}H_{18}O_2S$	$C_{23}H_{21}NS_2$	$C_{16}H_{21}NS_2$
Formula weight [g mol-1]	346.44	375.55	291.47
Crystal color, habit	pale yellow, prism	yellow, plate	colorless, tablet
Crystal dimensions [mm]	0.17 × 0.20 × 0.25	0.07 × 0.27 × 0.27	0.08 × 0.20 × 0.35
Temperature [K]	160(1)	160 (1)	160(1)
Crystal system	orthorhombic	orthorhombic	monoclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1/n$
Z	4	4	4
Reflections for cell determination	40845	21978	24601
2θ range for cell determination [°]	4 – 55	4 – 60	4 – 60
Unit cell parameters a [Å]	5.5779(3)	9.2847(2)	6.4888(1)
b [Å]	8.1397(5)	12.7753(2)	16.6408(3)
c [Å]	38.894(2)	15.7321(3)	14.2958(2)
β [°]	90	90	99.210(1)
V [Å^3]	1765.9(2)	1866.06(6)	1523.74(4)
D_x [g cm-3]	1.303	1.337	1.270
μ(MoK_α) [mm-1]	0.195	0.292	0.336
Scan type	ϕ and ω	ϕ and ω	ϕ and ω
2θ (max) [°]	55	60	60
Transmission factors (min; max)	0.844; 0.954	0.908; 0.982	0.895; 0.979
Total reflections measured	14153	36680	42595
Symmetry independent reflections	3957	5451	4459
Reflections with $I > 2\sigma(I)$	2650	4864	3473
Reflections used in refinement	3955	5450	4457
Parameters refined	228	237	174
Final $R(F)$ [$I > 2\sigma(I)$ reflections]	0.0630	0.0338	0.0404
$wR(F^2)$ (all data)	0.1608	0.0783	0.1104
Weighting parameters (a; b)[a]:	0.0649; 1.0748	0.0348; 0.4491	0.0517; 0.5980
Goodness of fit	1.040	1.053	1.040
Final Δ_{max}/σ	0.001	0.001	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.55; -0.24	0.21; -0.31	0.31; -0.38

[a]) $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$ where $P = (F_o^2 + 2F_c^2)/3$

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Chapter 5

1,5-Dipolar Electrocyclizations of Thiocarbonyl Ylides Bearing C=N Groups: Reactions of *N*-[(Dimethylamino)methylene]thiobenzamide and 2-(Dimethylhydrazono)-1-phenylethane-1-thione with Diazo Compounds[1])

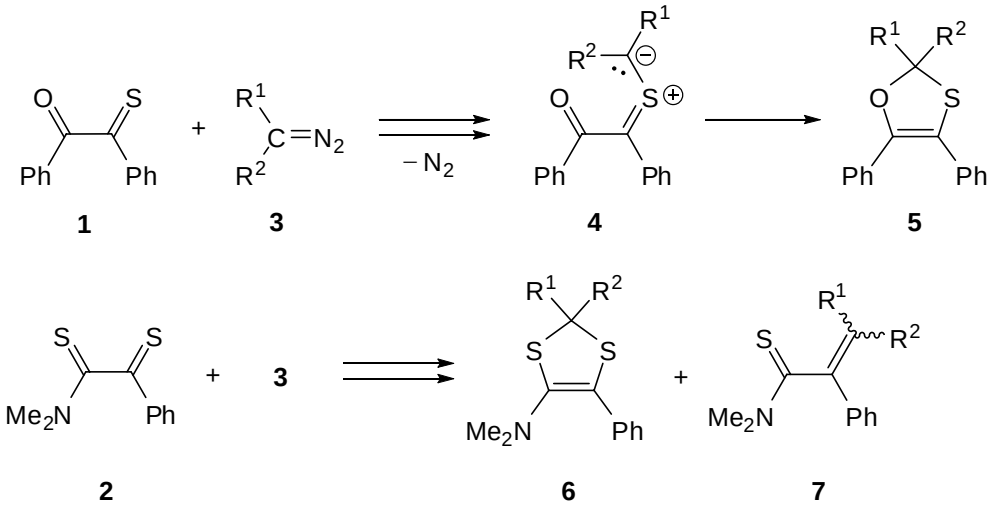
The reactions of thiobenzamide **8** with diazo compounds proceeded *via* reactive thiocarbonyl ylides as intermediates, which underwent either a 1,5-dipolar electrocyclization to give the corresponding five-membered heterocycles, *i.e.,* 4-amino-4,5-dihydro-1,3-thiazole derivatives (**10a**, **10b**, **10c**, *cis*-**10d**, and *trans*-**10d**) or a 1,3-dipolar electrocyclization to give the corresponding thiiranes as intermediates, which underwent a S_Ni'-like ring opening and subsequent 5-*exo*-*trig* cyclization to yield the isomeric 2-amino-2,5-dihydro-1,3-thiazole derivatives (**11a**, **11b**, **11c**, *cis*-**11d**, and *trans*-**11d**). In general, isomer **10** was formed in higher yield than isomer **11**. In the case of the reaction of **8** with phenyldiazomethane (**3d**), a mixture of two pairs of diastereoisomers was formed, whereof two, namely *cis*-**10d** and *trans*-**10d**, could be isolated as pure compounds. The isomers *cis*-**11d** and *trans*-**11d** remained as a mixture. In the reactions of the α-thioxohydrazone **9** with diazo compounds **3b** and **3d**, the main products were the alkenes **18** and **23**. Their formation was rationalized by a 1,3-dipolar electrocyclization of the corresponding thiocarbonyl ylide and subsequent desulfurization of the intermediate thiirane. As minor products, 2,5-dihydro-1,3-thiazol-5-amines **21** and **24** were obtained, which have been formed by 1,5-dipolar electrocyclization of the thiocarbonyl ylide followed by a 1,3-shift of the dimethylamino group.

1. Introduction. – The concept of the 1,5-dipolar electrocyclization as a tool for the synthesis of five-membered heterocycles has been proposed 25 years ago [1][2]. Since, we have shown that thiocarbonyl ylides, which bear a carbonyl group at the C(α)-atom, undergo this cyclization to give 1,3-oxathioles [3][4] (see also [5][6]). These thiocarbonyl ylides were generated *in situ* by the reaction of thiocarbonyl derivatives with α-diazo carbonyl compounds. Very recently, we reported on the reaction of α-thioxocarbonyl

[1]) D. H. Egli, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2007**, *90*, 86.

derivatives with diazo compounds [7]. We were mostly interested in systems, in which the conjugate π-system consisted of a C=O or a C=S group, *i.e.*, in reactions of α-thioxoketone **1** and α-thioxothioamide **2** (*Scheme 1*).

Scheme 1



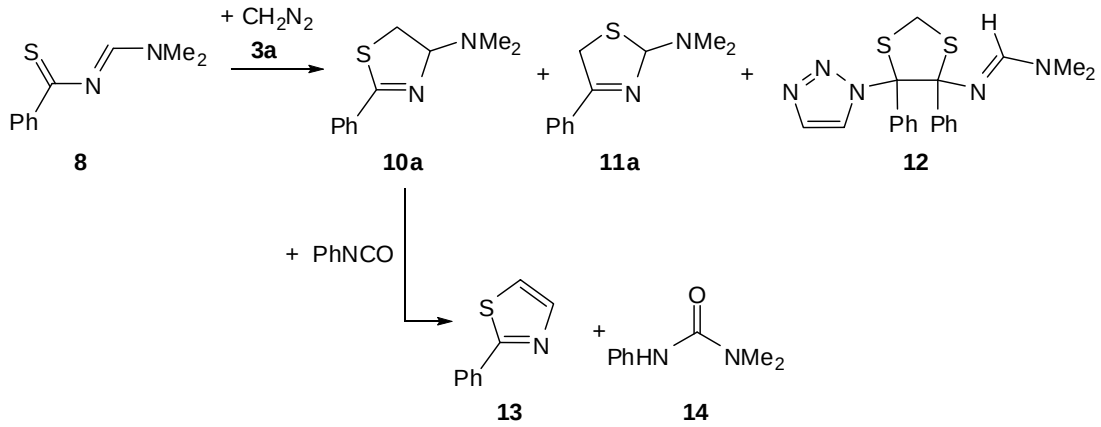
The reactions with diazo compounds **3** followed all the same pathway: 1,3 dipolar cycloaddition to give a 2,5-dihydro-1,3,4-thiadiazole, N_2 elimination by cycloreversion to produce thiocarbonyl ylides **4**, and 1,5-dipolar electrocyclization. The resulting products are either 1,3-oxathioles **5** or 1,3-dithioles **6**. Some thiirane side products, which were formed by a competing 1,3-dipolar electrocyclization, were unstable, and elimination of sulfur led to the corresponding alkenes, *e.g.* **7**.

With the aim of extending the scope of this reaction, we used thiocarbonyl compounds, which possess a conjugated system containing a N-atom. Since *N*-[(dimethylamino)-methylene]thiobenzamide (**8**) is not only readily available, but also stable, and thus allows for a precise calculation of the yield[2]), we used it as a starting material in the present work. Because we were interested in systems with the N-atom in different positions, reactions of 2-(dimethylhydrazono)-1-phenylethanethione (**9**) were also investigated. Although **9** showed a few drawbacks concerning stability and yield calculation we used it because of the relatively simple four-step synthesis. The results of the reactions with **8** and **9** are presented below.

[2]) Because of unstable starting materials it was a problem to calculate correct yields for the reactions described in [7].

2. Results and Discussion. – 2.1. *Reactions with* N-*[(Dimethylamino)-methylene]thio-benzamide* (**8**). In 1989, *Danion et al.* [8] have shown that the reaction of **8** with diazomethane (**3a**) in Et_2O in the dark led to three products **10a**, **11a** and **12** (*Scheme 2*). The correlation of the spectroscopic data with the corresponding structures was supported by the conversion of **10a** with phenylisothiocyanate in refluxing benzene to give the known 1,3-thiazol **13** and *N*,*N*-dimethyl-*N*'-phenylurea **14** (*Scheme 2*).

Scheme 2



On closer inspection of this result, we became convinced that the correlation of the structures and data requires verification, because an additional structure also corresponds with the given data. Instead of **11a**, the isomeric structure **10a'** (*Fig. 1*) could be generated by a 1,3-H shift in **10a**. The corresponding data of **10a'** and **11a** are expected to be quite similar, but the results of NOE experiments by irradiation of the Me_2N group would be distinctive differ. Whereas **10a** and **11a** should show a positive NOE, no NOE would be observed in the case of **10a'** (*Fig. 1*).

Therefore, we repeated the experiment with **8** and **3a** in Et_2O and obtained two isomeric dihydro-1,3-thiazoles in accordance with ref. [8]. Both products showed a positive NOE of the methine H-atom on irradiation of Me_2N, *i.e.*, both molecules contain the structure fragment CH–NMe_2 and, therefore, the assignment made by *Danion et al.* is correct indeed. The formation of **10a'** can be excluded.

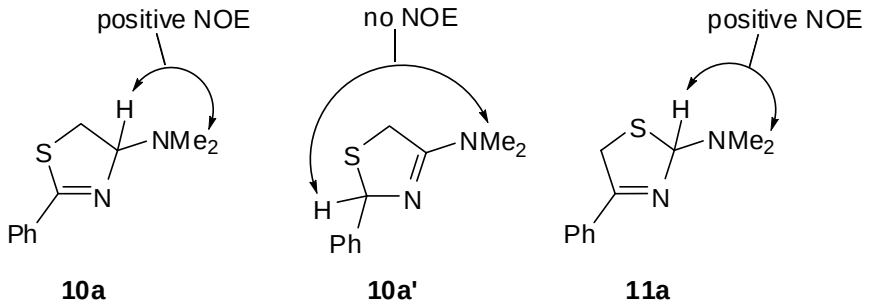
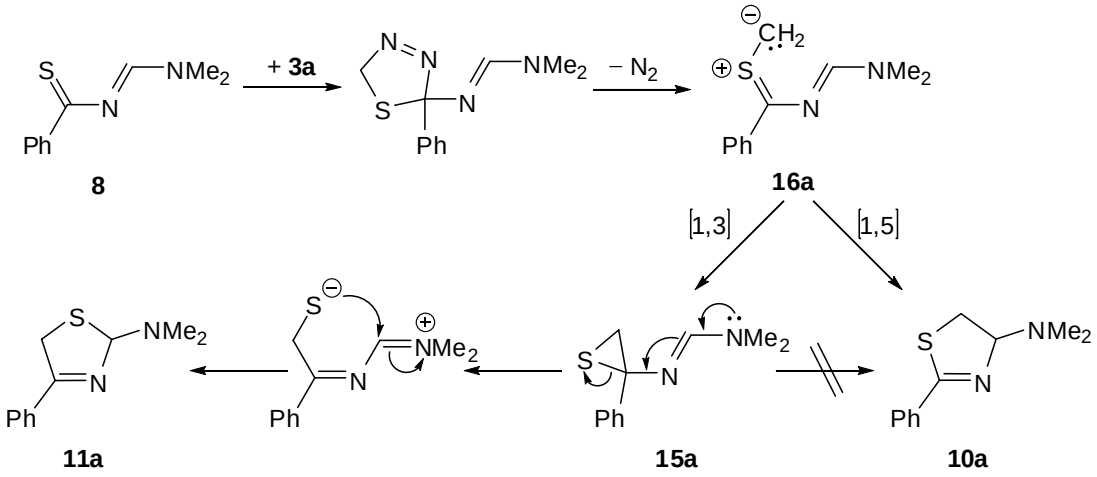


Fig. 1 *NOE-signals of* **10a**, **10a'** *and* **11a**.

However, the reaction pathway proposed by *Danion et al.*, in which **10a** and **11a** are formed *via* an intermediate thiirane **15a**, is not in accordance with the general experience of such reactions. We assume that the intermediate thiocarbonyl ylide **16a** is the origin of both compounds **10a** and **11a** (*Scheme 3*). Whereas the formation of **11a** can be explained *via* a 1,3-dipolar electrocyclization to give **15a**, followed by a S_Ni'-like ring opening and subsequent 5-*exo-trig* cyclization, as proposed by *Danion et al.,* **10a** is formed *via* a 1,5-dipolar electrocyclization of **16a**. This pathway seems to be much more reliable as there is no C,C-bond cleavage of the thiirane ring known to give thiocarbonyl ylides. Rather thiocarbonyl ylides are the usual intermediates of reactions of thioketones with diazo compounds [5][6].

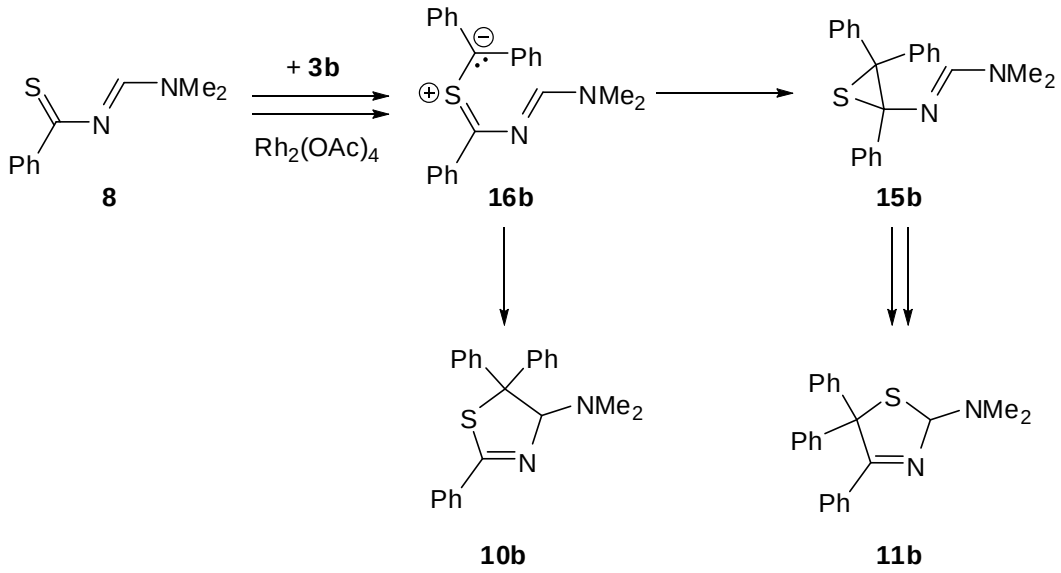
Scheme 3



The reaction of **8** with diphenyldiazomethane (**3b**) was carried out in CH_2Cl_2 at room temperature in the presence of catalytic amount of $Rh_2(OAc)_4$ and yielded two products. Based on previous experiences from experiments with thiocarbonyl ylides [7], we assumed

that the reaction would lead to an intermediate thiocarbonyl ylide **16b**, which would undergo either a 1,3-dipolar electrocyclization to give the thiirane **15b** and, by subsequent S_Ni'-ring opening and 1,5-cyclization, the 2,5-dihydro-1,3-thiazol **11b**, or a 1,5-dipolar electrocyclization to yield the corresponding 4,5-dihydro-1,3-thiazol **10b** (*Scheme 4*).

Scheme 4



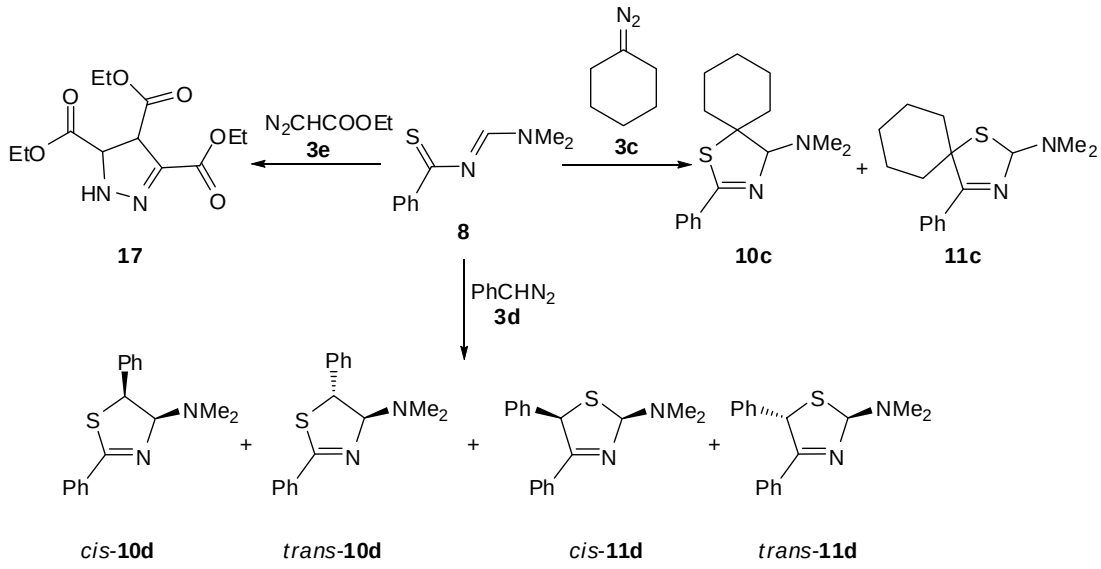
The ^{13}C-NMR spectra of the two isolated products showed that we could exclude structure **15b**, because the expected *d* for the amidine C-atom at about 155 ppm was missing (see experimental part). The spectra of both compounds again were very similar with only small deviations of 5-10 ppm for some signals. The NOE experiment of **10b** showed that the Me_2N group in **10b** has to be close to the H-atom, which absorbed at 6.84 ppm. In the case of **11b**, the NOE experiment showed the analogous response of an H-atom bonded to the heterocycle, therefore, an isomer of type **10a'** (*Fig. 1*) can be excluded. By 'inadequate-NMR measurements' of **10b** it has been shown that $CHNMe_2$ is connected directly to another C-atom of the ring. In compound **11b**, no such coupling would be observed. Unfortunately, it was not possible to crystallize the two products as they remained as oily substances. Obviously, the 1,5-dipolar electrocyclization is preferred to a 1,3-dipolar electrocyclization, since the yield of **10b** (49%) is significantly higher than that of **11b** (30%).

Similar to the reaction of **8** with **3b**, treatment with diazocyclohexane (**3c**) led to two products **10c** and **11c** (*Scheme 5*). The latter proved to be unstable and could not be isolated in pure form. In contrast to the previous experiments, the reaction takes place

spontaneously and, therefore, there was no need to add Rh-catalyst. In the crude NMR spectrum, the products showed the already known pattern of the **10a**/**11a** mixture but the ratio of **10c** to **11c** rose to 3:1 (*Scheme 5*).

The next diazo compound, which was selected for the reaction with **8**, was phenyldiazomethane (**3d**). In Et_2O/toluene at room temperature, a spontaneous reaction occurred, which after 5 d led to a mixture of four isomeric products, but only three of them, namely *cis*-**10d**, *cis*-**11d**, and *trans*-**11d**, could be isolated after chromatographic work up (SiO_2, hexane/AcOEt/Et_3N; *Scheme 5*). The analogous reaction of **8** with **3d** in THF, catalyzed by $Rh_2(OAc)_4$, and work up without using Et_3N as an additive led to only one product, namely the fourth isomer, *i.e., trans*-**10d**, of the reaction described above (see experimental part). The reasons for the different results are not clear. A possible explanation could be that under acidic work up conditions (SiO_2 without Et_3N), the isomers *cis*-**11d** und *trans*-**11d** decomposed and *cis*-**10d** isomerized to *trans*-**10d**. With respect to the thermodynamic stability, the *trans*-product should be more stable than the *cis*-isomer.

Scheme 5

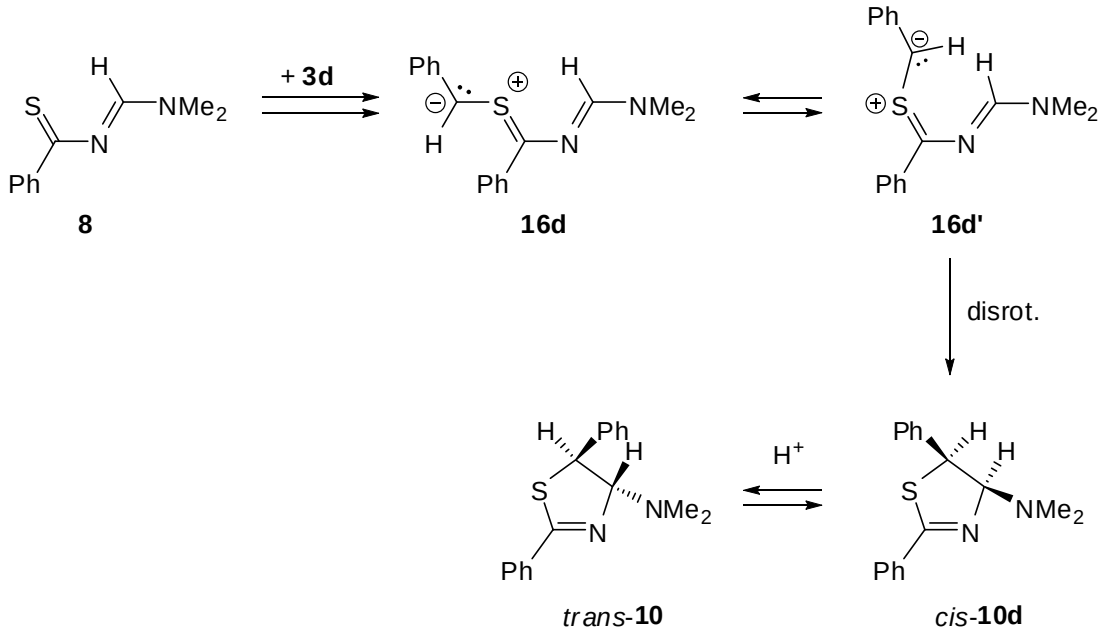


The assignment of the structures of the four isomers was achieved on the basis of the following data. First, 2D-NMR studies (HMBC) have shown a coupling between Me_2N and both H-atoms of the heterocycle, namely HC(4) and HC(5), of *trans*-**10d**. On the other hand, only one coupling (Me_2N, HC(2)) was observed in *cis*- and *trans*-**11d**. Second, the *cis*- and *trans*-isomers could be distinguished on the basis of their H,H-coupling constants. As a rule, the *cis* coupling in five-membered heterocycles is larger than the *trans* coupling [9]. Therefore, the smaller coupling constant of 4.4 Hz between HC(4) and HC(5) of *trans*-

10d (*cis*-**10d**, 7.6 Hz) indicates the *trans*-configuration.

An explanation of the formation of the thermodynamically less favored *cis*-**10d** is based on the selectivity rules for pericyclic reactions (see for example [10][11]). For steric reasons, the preferred structure of the thiocarbonyl ylide formed from **8** and **3d** should be **16d**, which is in equilibrium with **16d'** (*Scheme 6*). The disrotatory ring closure of the latter yields then *cis*-**10d**. The more stable *trans*-**10d** could be formed under the conditions of the acidic work up *via* a reversible 1,3-H shift.

Scheme 6



Surprisingly, the reaction of ethyl diazoacetate (**3e**) with **8** did not lead to the expected thiazole derivative. The only product, which could be isolated in traces, was **17**, the 'trimer' of the starting diazo compound (*Scheme 5*). Its structure was established by X-ray crystallography (*Fig. 2*). In the crystal structure, the two ester groups at the adjacent chiral centres have the *trans* configuration. The NH group forms an intermolecular H-bond with one of the ester carbonyl O-atoms of an adjacent molecule and thereby links the molecules into extended chains, which run parallel to the [100] direction and can be described by a graph set motif [12] of C(6).

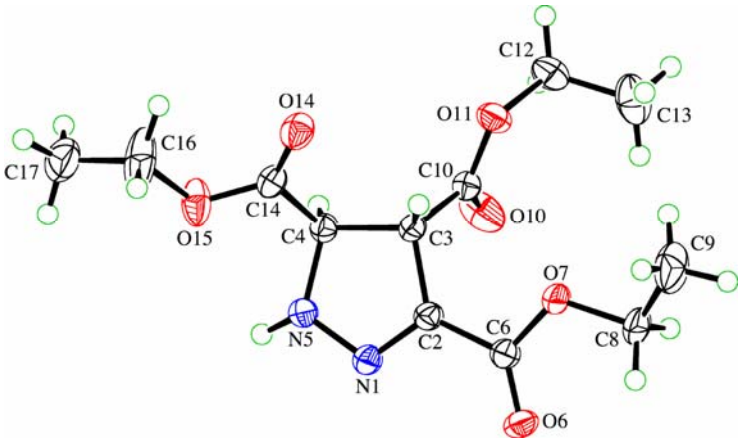
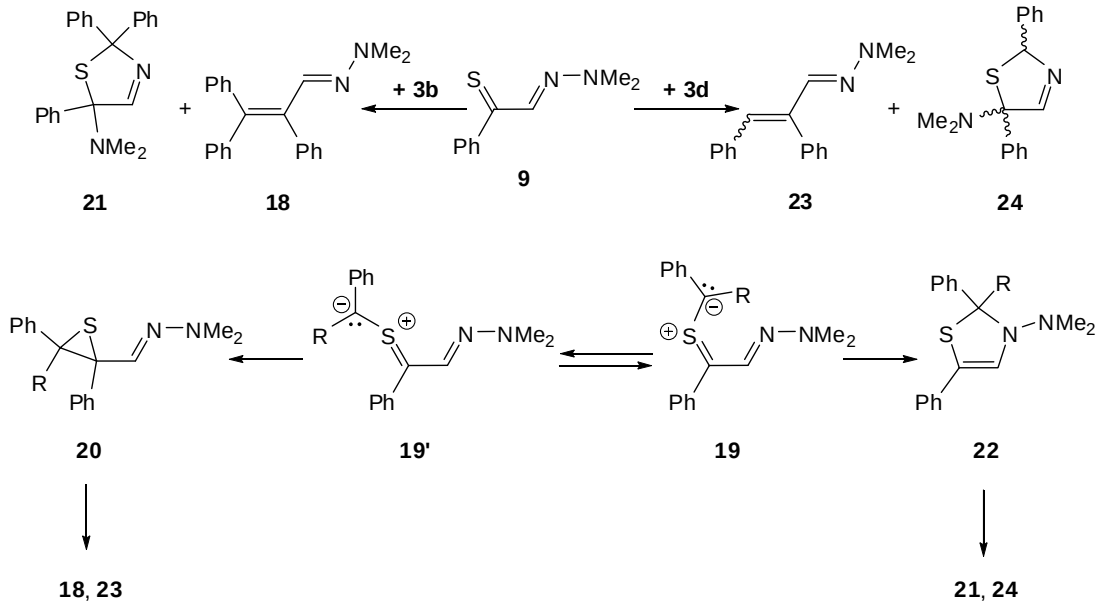


Fig. 2 *ORTEP Plot* [13] *of the molecular structure of* **17** (50% probability ellipsoids, arbitrary numbering of atoms)

The described results obtained with **8** show that this starting material is relatively unreactive and, therefore, the reaction with less reactive diazo compounds has to be catalyzed by $Rh_2(OAc)_4$ or the reaction time has to be increased. Whereas in the reaction of **8** with **3a** 46% of the products (**10a** + **11a**) could be isolated, no reaction took place with **3b** without addition of catalyst. In the case of **3e**, no formation of a thiocarbonyl ylide was observed. Instead, dimerization of the generated carbenoïd yielded diethyl fumarate [14], which underwent a 1,3-dipolar cycloaddition with **3e** to give **17**.

2.2. *Reactions with 2-(Dimethylhydrazono)-1-phenylethanethione* (**9**). The reaction of **9** with **3b** in benzene at room temperature gave two products. The first one was identified as *N*,*N*-dimethyl-*N'*-(2,3,3-triphenylprop-2-enylidene)hydrazine (**18**). The reaction mechanism of its formation, in analogy with previous cases, is supposed as follows: 1,3-dipolar cycloaddition and elimination of N_2 yields the thiocarbonyl ylide of type **19'**, which undergoes a 1,3-dipolar electrocyclization to give the corresponding thiirane **20**. Finally, desulfurization of the latter leads to **18** (*cf.* [7]). The second product was isolated in small yields and turned out, surprisingly, to be *N*,*N*-dimethyl-*N*-(2,2,5-triphenyl-2,5-dihydrothiazol-5-yl)amine (**21**). It apparently results from a rearrangement of the primarily formed intermediate 3-amino-1,3-thiazole **22** (R = Ph). In this case, unlike in the reactions with **8**, the Me_2N group is bound to the N(3) atom. A 1,3-shift of the amino substituent then leads to the 2,5-dihydro-1,3-thiazol **21** (*Scheme 7*).

Scheme 7



The structures of **18** and **21** have been established by X-ray crystallography (*Fig. 3*). The conjugated π-system in **18** from C(1) to N(4), including N(5), C(7), C(13), and C(19) is almost planar. All phenyl substituents in compound **18** are twisted out of this plane because of steric reasons (torsion angles C(2)–C(1)–C(7)–C(8) 52.7(2)°, C(2)–C(1)–C(13)–C(18) 44.0°, and C(1)–C(2)–C(19)–C(20) 55.1(2)°). In the case of **21**, the asymmetric unit contains two symmetry-independent molecules, each of which is disordered by inversion of the entire molecule about its centre of gravity. The ratio of the major orientation of each molecule to the minor orientation is about 93:7. The crystals are also inversion twins.

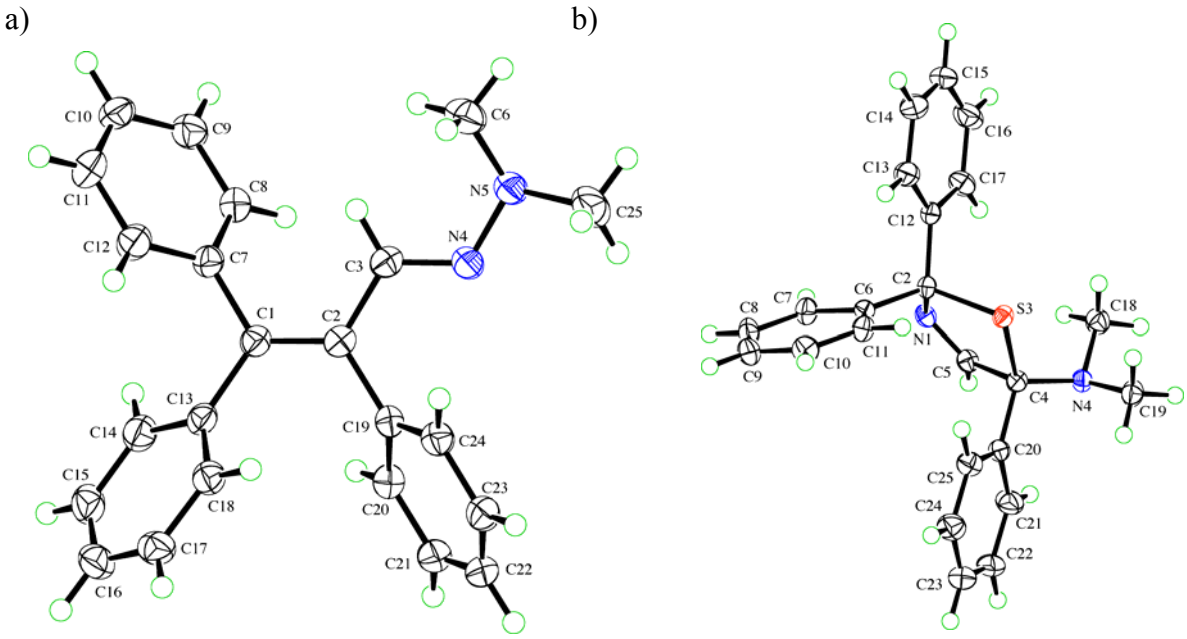


Fig. 3 *ORTEP Plot* [13] *of the molecular structure of a)* **18** *and b) one of the independent molecules of* **21** (50% probability ellipsoids, arbitrary numbering of atoms)

The analogous reaction of **9** with **3d** gave a complex mixture of products, which consisted of two pairs of diastereoisomers at least. The (*E*/*Z*)-isomers of *N*,*N*-dimethyl-*N'*-(2,3-diphenylprop-2-enylidene)hydrazine (**23**) and the *cis*/*trans*-isomers of *N*,*N*-dimethyl-*N*-(2,5-diphenyl-2,5-dihydrothiazol-5-yl)amine (**24a**,**b**) are the likely products, which could be separated partially by CC and MPLC. The structures were elucidated on the basis of the NMR and mass spectra. Furthermore, one of the diastereoisomers of **24**, *i.e. trans*-**24**, could be crystallized and the X-ray crystal-structure was determined successfully (*Fig. 4*). In the crystal, the heterocyclic ring has a shallow envelope conformation with S(3) as the envelope flap. The phenyl substituents lie *cis* to one another.

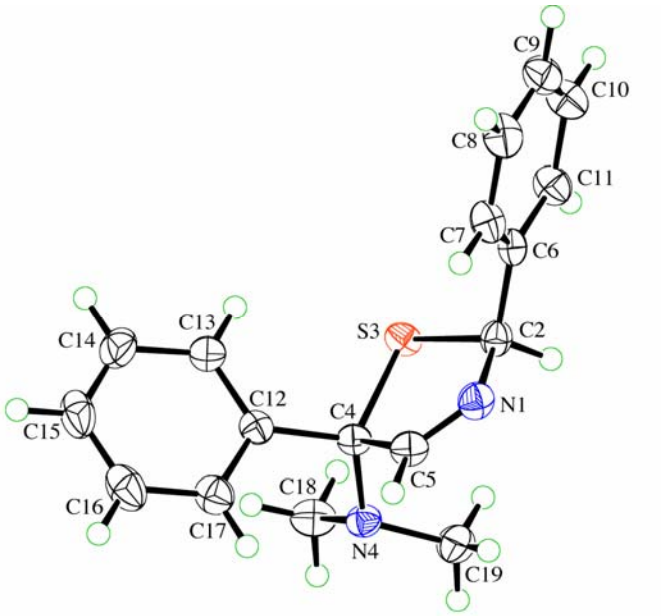


Fig. 4 *ORTEP Plot* [13] *of the molecular structure of trans*-**24** (50% probability ellipsoids, arbitrary numbering of atoms)

The reactions of **9** with **3b** and **3d**, respectively, showed that the intermediate thiocarbonyl ylide **19** reacts only to a minor extent to the five-membered ring. The preferred reaction of **19** is the 1,3-dipolar electrocyclization, which leads to an intermediate thiirane **20**, and subsequent desulfurization yields the alkenes.

3. Conclusions. – The presented results show that the two thiocarbonyl compounds **8** and **9** with a conjugated C=N group react with diazo compounds **3** to give the corresponding thiocarbonyl ylides of type **16** and **19**, respectively, with an extended π-system. In the case of **8** and the less reactive **3b**, the reaction has to be catalyzed by $Rh_2(OAc)_4$. Whereas in the non-catalyzed reaction a 1,3-dipolar cycloaddition to give the corresponding 2,5-dihydro-1,3,4-thiadiazole and subsequent N_2-elimination is the likely reaction mechanism of the formation of the thiocarbonyl ylide, an initial Rh-catalyzed N_2-elimination to give a carbenoïd, which adds to the C=S group, leads to the intermediate 1,3-dipoles in the catalyzed reactions [5][6]. The thiocarbonyl ylides of type **16**, which have been generated from **8**, undergo competitive 1,5- and 1,3-dipolar electrocyclizations and yield dihydro-1,3-thiazole and thiirane derivatives, respectively. On the other hand, the main reaction of the isomeric thiocarbonyl ylides **19** is the 1,3-dipolar electrocyclization, which leads to thiiranes **20**.

We thank the analytical units of our institute for spectra and analyses, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for financial support.

Experimental Part

1. *General.* See [7]. IR Spectra in KBr unless otherwise stated. ^{1}H- and ^{13}C-NMR Spectra: *Avance DRX-500* (500 and 125 MHz, resp.), and *Avance DRX-600* (600 and 150 MHz, resp.). M.p.: *Büchi* B-540.

2. *Starting Materials.* All thiocarbonyl derivatives and their precursors and all diazo compounds were prepared following known protocols: diazomethane (**3a**) [15], diphenyldiazomethane (**3b**) [16], diazocyclohexane (**3c**) [17], phenyldiazomethane (**3d**) [18], *N*-[(dimethylamino)methylene]thiobenzamide (**8**) [19], 2-(dimethylhydrazono)-1-phenylethanethione (**9**) [20][21]. All other reagents are commercially available.

3. *Yields*. As **9** and almost all diazo compounds are only stable in solution and the diazo compounds were often used in excess, the yields of the corresponding reactions were approximated. They are based on experience [7] or on the volume of N_2 evolved.

4. *General Procedure A* (*GP A*): To a soln. of a thiocarbonyl compound (1.8-5.2 mmol) in CH_2Cl_2, Et_2O or THF (20-100 ml), the diazo compound (3-8 mmol) in toluene, benzene, or Et_2O (30-150 ml) was added in several portions by means of a dropping funnel, or, in the case of **3a,** by means of a *Pasteur* pipette. After total conversion of the thiocarbonyl compound, monitored either by TLC (treated during 20 s with a soln. of Et_2O and 1% of Et_3N), color change or evolution of N_2[3]), the solvent was evaporated and the mixture was analyzed and purified by chromatography using silica gel, which had been treated with 3% Et_3N. Furthermore, the solvent was doped with 1% of Et_3N.

5. *Reaction of* N-*[(Dimethylamino)methylene]thiobenzamide* (**8**) *with diazoalkanes.*

5.1. N,N-*Dimethyl*-N-*(2-phenyl-4,5-dihydro-1,3-thiazol-4-yl)amine* (**10a**) and N,N-*Dimethyl*-N-*(4-phenyl-2,5-dihydro-1,3-thiazol-2-yl)amine* (**11a**). According to *GP A,* a soln. of **8** (772 mg, 4 mmol) in Et_2O (30 ml) and **3a** (*ca*. 6 mmol) in Et_2O (30 ml) were used. After 3 d at r.t. in the dark, the mixture was separated by CC (hexane/AcOEt 5:1) to give 173 mg (*ca.* 21%) of **10a** and 206 mg (*ca.* 25%) of **11a**. Data of **10a**: Yellowish oil. IR (neat): 3081*w*, 3060*m*, 3028*m*, 2970v*s*, 2939v*s*, 2864v*s*, 2829v*s*, 2784*s*, 1688*w*, 1607v*s*, 1578*s*, 1490*s*, 1473*s*, 1448v*s*, 1358v*s*, 1297v*s*, 1272v*s*, 1233v*s*, 1196*s*, 1177*m*, 1156*m*, 1119*s*,

[3]) The evolution of N_2 was determined volumetrically using a gas burette attached to the reaction vessel.

1073v*s*, 1042v*s*, 999v*s*, 949v*s*, 766v*s*, 690v*s*, 624*s*. ^{1}H-NMR: 7.88–7.85 (*d*-like, 2 arom. H); 7.47–7.38 (*m*, 3 arom. H); 5.56 (*dd*, *J* = 6.7, 2.4, HC(4)); 3.51 (*dd*, *J* = 9.1, 2.7, 1 H of CH_2); 3.28 (*dd*, *J* = 6.7, 5.1, 1 H of CH_2); 2.44 (*s*, Me_2N). ^{13}C-NMR: 167.0 (*s*, C(2)); 133.1 (*s*, 1 arom. C); 131.2, 128.3, 128.3 (3*d*, 5 arom. CH); 97.3 (*d*, C(4)); 40.4 (*t*, CH_2); 34.5 (*q*, Me_2N). CI-MS (NH_3): 207 (100, $[M + 1]^+$), 162 (36, $[M - Me_2NH]^+$), 104 (17).

Data of **11a**: Yellowish crystals. M.p. 64–67°. IR: 3126*w*, 3058*m*, 3032*w*, 2922*m*, 2805*w*, 1726*m*, 1683*m*, 1644v*s*, 1579*m*, 1489*s*, 1445*s*, 1414*s*, 1354*m*, 1274*m*, 1254*m*, 1226*m*, 1185*m*, 1159*w*, 1116*m*, 1061*s*, 1042*s*, 1030*s*, 1009*m*, 775*s*, 746*s*, 732*s*, 696*s*. ^{1}H-NMR: 7.95–7.92 (*d*-like, 2 arom. H); 7.49–7.40 (*m*, 3 arom. H); 7.08 (*dd*, *J* = 5.2, 1.9, HC(4)); 4.34 (*dd*, *J* = 16.3, 1.9, 1 H of CH_2); 4.22 (*dd*, *J* = 16.3, 5.2, 1 H of CH_2); 2.25 (*s*, Me_2N). ^{13}C-NMR: 168.9 (*s*, C(2)); 133.1 (*s*, 1 arom. C); 131.4, 128.5, 128.5 (3*d*, 5 arom. CH); 107.3 (*d*, C(4)); 41.3 (*t*, CH_2); 39.0 (*q*, Me_2N). CI-MS (NH_3): 206 (18, $M^{+\cdot}$), 174 (100, $[M - S]^+$), 161 (94, $[M - Me_2N]^+$), 134 (82, $[M - NHCHNMe_2]^+$), 103 (58, Ph $CN^{+\cdot}$).

If the chromatographic work up was carried out without addition of Et_3N as described in [8], only **11a** was isolated.

5.2. N,N-*Dimethyl*-N-*(2,5,5-triphenyl-4,5-dihydro-1,3-thiazol-4-yl)amine* (**10b**) *and* N,N-*Dimethyl*-N-*(4,5,5-triphenyl-4,5-dihydro-1,3-thiazol-2-yl)amine* (**11b**). According to *GP A,* a suspension of **8** (360 mg, 1.87 mmol) in CH_2Cl_2 (20 ml) and a soln. of **3b** (*ca*. 2.5 mmol) in benzene (20 ml) were used. To the stirred mixture at r.t., a catalytic amount (20 mg) of $Rh_2(OAc)_4$ was added. After *ca.* 16 h, the mixture was separated by CC (hexane/AcOEt 20:1 to 5:1): 328 mg (0.92 mmol, 49%) of **10b** and 200 mg (0.56 mmol, 30%) of **11b**. Data of **10b**: Yellowish oil. R_f = 0.5; hexane/AcOEt 8:1. IR: 3057*m*, 3027*m*, 2935*s*, 2865*s*, 2831*s*, 2786*m*, 1805*w*, 1733*w*, 1596*s*, 1575*s*, 1491v*s*, 1472*m*, 1445v*s*, 1311*m*, 1275*s*, 1227*s*, 1176*m*, 1156*m*, 1083*s*, 1062v*s*, 1040v*s*, 994v*s*, 944v*s*, 920*m*, 901*m*, 888*m*, 828*m*, 765v*s*, 752v*s*, 723v*s*, 694v*s*, 632*m*, 623*s*. ^{1}H-NMR: 7.87–7.84 (*q*-like, 2 arom. CH); 7.43–7.07 (*m*, 13 arom. CH); 6.01 (*s*, HC(2)); 2.19 (*s*, Me_2N). ^{13}C-NMR: 166.1 (*s*, C(4)); 149.1, 140.1, 133.2 (3*s*, 3 arom. C); 131.4, 129.9, 128.5, 128.3, 128.3, 127.3, 126.9, 126.9, 126.4 (9*d*, 15 arom. CH); 100.9 (*d*, C(2)); 74.4 (*s*, C(5)); 41.3 (*q*, Me_2N). CI-MS (NH_3): 359 (100, $[M + 1]^+$), 314 (39, $[M - Me_2NH]^+$), 224 (37).

Data of **11b**: Yellowish oil. R_f = 0.3; hexane/AcOEt 8:1. IR: 3056*m*, 3028*w*, 2977*m*, 2942*m*, 2860*m*, 2825*m*, 2779*m*, 1807*w*, 1734*w*, 1680*w*, 1624*s*, 1599*s*, 1545*m*, 1489*s*, 1470*s*, 1445v*s*, 1352*s*, 1289*m*, 1257*s*, 1205*m*, 1179*s*, 1152*m*, 1081*s*, 1067*s*, 1043*s*, 1023v*s*, 1002*s*, 932*m*, 908*w*, 852*s*, 824*w*, 772*s*, 758*s*, 742v*s*, 695v*s*, 639*m*. ^{1}H-NMR: 7.52–7.49 (*d*-

like, 2 arom. H); 7.40–7.35 (*t*-like, 4 arom. H); 7.21–7.00 (*m*, 9 arom. H); 6.84 (*s*, HC(4)); 2.27 (*s*, Me_2N). ^{13}C-NMR: 171.2 (*s*, C(2)); 143.1, 142.8, 133.2 (3*s*, 3 arom. C); 130.5, 130.2, 129.4, 129.0, 128.0, 127.8, 127.7, 127.0, 126.9 (9*d*, 15 arom. CH); 101.5 (*d*, C(4)); 78.3 (*s*, C(5)); 39.8 (*q*, Me_2N). CI-MS (NH_3): 359 (10, $[M + 1]^+$), 327 (100, $[M - S + 1]^+$), 314 (5 $[M - Me_2NH]^+$), 193 (22).

5.3. N,N-*Dimethyl*-N-*(2-phenyl-1-thia-3-azaspiro[4.5]dec-2-en-4-yl)amine* (**10c**). According to *GP A,* a suspension of **8** (384 mg, 2 mmol) in CH_2Cl_2 (10 ml) and a soln. of **3c** (*ca.* 2.5 mmol) in CH_2Cl_2 (40 ml) were used. After 1 d at r.t., the mixture was separated by CC (hexane/AcOEt 10:1 to 5:1): 360 mg (67%) of **10c** and 120 mg (22%) of a mixture of **10c** and N,N-*dimethyl*-N-*(4-phenyl-1-thia-3-azaspiro[4.5]dec-3-en-2-yl)amine* (**11c**)[4]). Data of **10c**: Yellowish oil. IR (neat): 3061*m*, 3027*w*, 2930*vs*, 2855*vs*, 2833*vs*, 2790*s*, 2669*w*, 1808*w*, 1756*w*, 1688*w*, 1595*vs*, 1577*s*, 1491*m*, 1473*s*, 1447*vs*, 1404*w*, 1377*m*, 1295*s*, 1266*vs*, 1246*vs*, 1229*s*, 1212*m*, 1176*m*, 1156*m*, 1135*m*, 1091*s*, 1074*s*, 1042*vs*, 1025*vs*, 993*vs*, 958*s*, 940*s*, 909*m*, 858*s*, 766*vs*, 690*vs*, 625*m*. ^{1}H-NMR: 7.91–7.88 (*d*-like, 2 arom. H); 7.45–7.36 (*m*, 3 arom. H); 4.92 (*s*, HC(4)); 2.48 (*s*, Me_2N) 2.04–1.32 (*m*, 10 H, cyclohexyl). ^{13}C-NMR: 167.4 (*s*, C(2)); 133.8 (*s*, 1 arom. C); 131.0, 128.3, 128.1 (3*d*, 5 arom. CH); 101.5 (*d*, C(4)); 66.6 (*s*, C(5)); 42.3 (br. *q*, Me_2N); 40.9, 32.2, 26.3, 25.5, 24.2 (5*t*, 5 CH_2, cyclohexyl). EI-MS: 275 (10), 274 (47, $M^{+\cdot}$), 230 (7, $[M - Me_2N]^+$), 171 (28), 160 (100 $[M - S - cyclohexyl]^+$), 138 (18), 121 (11), 103 (24), 57 (84).
Data of **11c** (from a *ca.* 1:3 mixture of **10c**/**11c**). ^{1}H-NMR: 7.48–7.38 (*m*, 5 arom. H); 6.76 (*s*, HC(2)); 2.31 (*s*, Me_2N); 1.93–1.59 (*m*, 10 H, cyclohexyl). ^{13}C-NMR: 176.8 (*s*, C(4)); 135.0 (*s*, 1 arom. C); 129.0, 128.2, 127.9 (3*d*, 5 arom. CH); 100.3 (*d*, C(2)); 72.7 (*s*, C(5)); 39.3 (*s*, Me_2N); 38.1, 36.9, 25.2, 25.0, 24.5 (5*t*, 5 CH_2, cyclohexyl).

5.4. N,N-*Dimethyl*-N-*(*cis-*2,5-diphenyl-4,5-dihydro-1,3-thiazol-4-yl)amine* (*cis*-**10d**) and N,N-*Dimethyl*-N-*(*cis/trans-*4,5-diphenyl-2,5-dihydro-1,3-thiazol-2-yl)amine* (*cis*-**11d**, *trans*-**11d**). According to *GP A,* soln. of **8** (1 g, 5.2 mmol) in dry Et_2O (30 ml) and **3d** (*ca.* 8 mmol) in toluene (150 ml) were used. After 4 d at r.t. in the dark, the mixture was separated by CC (hexane/AcOEt 3:1) and MPLC (Et_2O/hexane 1:5): 362 mg (*ca.* 24%) of *cis*-**10d** (colorless oil) and 616 mg (*ca.* 43%) of a mixture of *cis*- and *trans*-**11d** (yellowish oil). Data of *cis*-**10d**: IR (neat): 3061*m*, 3028*m*, 2941*s*, 2866*s*, 2833*m*, 2786*m*, 2771*m*, 1680*w*, 1600*s*, 1577*s*, 1531*m*, 1493*s*, 1471*m*, 1447v*s*, 1420*m*, 1366*m*, 1312*s*, 1269*s*,

[4]) It was not possible to isolate **11c** as a pure compound.

1226*m*, 1177*m*, 1155*m*, 1068*s*, 1040*s*, 988*s*, 943*m*, 910*m*, 896*m*, 765v*s*, 731*s*, 694v*s*. ^{1}H-NMR: 7.96–7.93 (*d*-like, 2 arom. H); 7.49–7.23 (*m*, 8 arom. H); 5.20 (*d*, *J* = 7.6, HC(4)); 5.05 (*d*, *J* = 7.6, H(C(5)); 2.30 (*s*, Me_2N). ^{13}C-NMR: 166.2 (*s*, C(2)); 137.5, 133.4 (2*s*, 2 arom. C); 131.4, 128.5, 128.4, 128.3, 128.2, 127.6 (6*d*, 10 arom. CH); 99.2 (*d*, C(4)); 57.4 (*d*, C(5)); 42.8 (*q*, Me_2N). CI-MS (NH_3): 281 (8), 238 (100, $[M - Me_2NH + 1]^+$), 148 (20). Data of the mixture of *cis*-**11d** and *trans*-**11d**[5]): IR (neat): 3060*m*, 3027*m*, 2978*m*, 2944*s*, 2862*s*, 2825*s*, 2779*m*, 1635v*s*, 1599*m*, 1577*m*, 1494*s*, 1471*s*, 1448v*s*, 1355*s*, 1337*m*, 1317*m*, 1279v*s*, 1213*m*, 1177*s*, 1067v*s*, 1046v*s*, 1037v*s*, 1024v*s*, 1001*m*, 886*s*, 853*s*, 763v*s*, 729v*s*, 693v*s*, 630*s*, 585*m*, 546*s*. ^{1}H-NMR (*cis*-**11d**): 7.82–7.74 (*m*, 2 arom. H); 7.35–7.15 (*m*, 8 arom. H, HC(4)); 5.88 (*d*, *J* = 4.8, HC(5)); 2.32 (*s*, Me_2N). ^{13}C-NMR (*cis*-**11d**): 169.7 or 169.2 (*s*, C(2)); 141.7, 132.7 or 132.4 (2*s*, 2 arom. C); 130.9, 130.8, 129.7, 129.5, 129.4, 129.1, 128.9, 128.3, 128.0, 127.5, 127.4, 127.2 (12*d*, 10 arom. CH); 105.7 (*d*, C(4)); 61.6 (*d*, C(5)); 39.3 (*q*, Me_2N). ^{1}H-NMR (*trans*-**11d**): 7.82–7.74 (*m*, 2 arom. H); 7.35–7.15 (*m*, 8 arom. H); 7.10 (*d*, *J* = 2.6, HC(4)); 5.97 (*d*, *J* = 2.6, HC(5)); 2.38 (*s*, Me_2N). ^{13}C-NMR (*trans*-**11d**): 169.7 or 169.2 (*s*, C(2)); 141.8, 132.7 or 132.4 (2*s*, 2 arom. C); 130.9, 130.8, 129.7, 129.5, 129.4, 129.1, 128.9, 128.3, 128.0, 127.5, 127.4, 127.2 (12*d*, 10 arom. CH); 105.2 (*d*, C(4)); 60.8 (*d*, C(5)); 39.8 (*q*, Me_2N). CI-MS (NH_3): 281 (6), 251 (100, $[M - S + 1]^+$), 238 (70, $[M - Me_2NH + 1]^+$), 148 (29).

5.5. N,N-*Dimethyl*-N-*(*trans-*2,5-diphenyl-4,5-dihydro-1,3-thiazol-4-yl)amine* (*trans*-**10d**). According to *GP A,* a soln. of **8** (592 mg, 3 mmol) in dry THF (20 ml) and **3d** (*ca*. 4 mmol) in toluene (80 ml) were used. To the stirred mixture at r.t., a catalytic amount (20 mg) of $Rh_2(OAc)_4$ was added. After 4 d, the mixture was separated by CC (hexane/AcOEt 4:1 to 1:4)[6]): 258 mg (*ca.* 41%[7])) of *trans*-**10d**. Yellowish-oily crystals. M.p. could not be determined. IR (neat): 3083*m*, 3061*s*, 3028*s*, 2972*s*, 2940*vs*, 2866*s*, 2833*s*, 2788*s*, 1808*w*, 1754*w*, 1716*w*, 1687*w*, 1608*vs*, 1600*vs*, 1579*s*, 1492*vs*, 1473*s*, 1449*vs*, 1361*s*, 1293*s*, 1272*s*, 1253*s*, 1228*s*, 1177*m*, 1158*s*, 1075*s*, 1040*vs*, 997*vs*, 960*s*, 936*s*, 865*m*, 766*vs*, 751*m*, 690*vs*. ^{1}H-NMR: 7.95–7.92 (*d*-like, 2 arom. H); 7.52–7.40 (*m*, 3 arom. H); 7.32–7.23 (*m*, 5 arom. H); 5.53 (*d*, *J* = 4.4, HC(4)); 4.80 (*d*, *J* = 4.4, H(C(5)); 2.45 (*s*, Me_2N).

[5]) On the basis of 2D-NMR experiments (HMBC) some signals could be assigned to the structures of *cis*-**11d** and *trans*-**11d**. The signals of the aromatic C-atoms and the quaternary C-atoms could not be correlated.

[6]) In the work up procedure no Et_3N was used.

[7]) *Ca*. 160 mg of the starting material **8** were recovered.

^{13}C-NMR: 167.3 (*s*, C(2)); 142.7, 131.5 (2*s*, 2 arom. C); 133.1, 128.9, 128.6[8]), 127.6, 127.4 (5*d*, 10 arom. CH); 106.2 (*d*, C(4)); 55.7 (*d*, C(5)); 40.5 (*q*, Me_2N). CI-MS (NH_3): 284 (21), 283 (100, $[M + 1]^+$), 238 (45, $[M - Me_2NH + 1]^+$), 148 (21).

5.6. *Experiment with Ethyl Diazoacetate* (**3e**). According to *GP A,* a suspension of **8** (380 mg, 2 mmol) in THF (20 ml) and a soln. of **3e** (*ca*. 4 mmol) in CH_2Cl_2 (40 ml) were used. To the stirred mixture, a catalytic amount (*ca.* 20 mg) of $Rh_2(OAc)_4$ was added. After 10 d at r.t., the mixture was separated by CC (hexane/AcOEt 4:1): 450 mg of a complex mixture of products resulting from decomposition and *ca.* 15 mg triethyl *trans*-4,5-dihydro-1*H*-pyrazole-3,4,5-tricarboxylate (**16**).

Crystals suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2/pentane by slow evaporation of the solvent.

6. *Reactions of 2-(Dimethylhydrazono)-1-phenylethanethione* (**9**) *with Diazoalkanes.*

6.1. N,N-*Dimethyl*-N*'-(2,3,3-triphenylprop-2-enylidene)hydrazine* (**18**) *and* N,N-*Dimethyl*-N-*(2,2,5-triphenyl-2,5-dihydro-1,3-thiazol-5-yl)amine* (**21**). To a soln. of freshly prepared **9** (*ca.* 1.6 mmol) in benzene (10 ml), a purple soln. of **3b** (*ca.* 2.5 mmol) in benzene (20 ml) was added drop-wise. After stirring for 1 h at r.t., purification of the crude mixture by SC (hexane/AcOEt 15:1) and MPLC (hexane/MeOH 90:5) afforded a mixture of two products, which were separated by crystallization from hexane/AcOEt/Et_2O affording 234 mg of **18** (30%) and 60 mg (7%) of **21**. Data of **18**: Pale-brownish crystals. M.p. 176–177°. IR: 3056*w*, 3027*w*, 2992*w*, 2970*w*, 2947*m*, 2867*m*, 2828*m*, 2783*w*, 1805*w*, 1664*m*, 1596*w*, 1580*w*, 1558*w*, 1488*s*, 1467*m*, 1445v*s*, 1175*m*, 1082*m*, 1073*m*, 1033*m*, 1009v*s*, 932*m*, 923*m*, 902*s*, 873*m*, 758v*s*, 697v*s*, 648*s*, 637*s*. ^{1}H-NMR: 7.36–6.85 (*m*, 15 arom. H and 1 =CH); 2.72 (*s*, Me_2N). ^{13}C-NMR: 142.8, 142.4, 139.5 (3*s*, 3 arom. C); 137.8 (*s*, 1 =C); 136.5 (br. *s*, 1 =C, 1 =CH); 131.7, 131.0, 130.9, 127.9, 127.2, 127.1, 126.2, 126.0 (8*d*, 15 arom. CH); 42.6 (*q*, Me_2N). CI-MS (NH_3): 327 (100, $[M + 1]^+$), 284 (16, $[M - Me_2N + 1]^+$), 203 (12), 178 (19), 160 (15), 158 (13).

Crystals suitable for the X-ray crystal-structure determination were grown from hexane/AcOEt/Et_2O by slow evaporation of the solvent.

Data of **21**: Colorless crystals. M.p. 135–137°. IR: 3063*w*, 3026*w*, 2992*w*, 2970*m*, 2946*m*, 2868*m*, 2828*m*, 2783*w*, 1956*w*, 1804*w*, 1664*m*, 1595*m*, 1580*w*, 1487*s*, 1467*s*, 1445v*s*, 1031*m*, 1009v*s*, 932*m*, 923*m*, 901v*s*, 873*m*, 757v*s*, 697v*s*, 661*m*, 648*s*, 637*s*, 615*m*. ^{1}H-

[8]) The intensity of this signal indicates absorption of 4 arom. CH.

NMR: 7.75 (*d*-like, 2 arom. H); 7.68–7.64 (*d*-like, 2 arom. H); 7.35–7.15 (*m*, 11 arom. H, HC(4)); 2.09 (*s*, Me_2N). ^{13}C-NMR: 162.7 (*d*, HC(4)); 146.2, 145.2, 139.8 (3*s*, 3 arom. C); 128.7, 128.5, 128.3, 127.9, 127.1, 127.1, 126.9, 126.5 (8*d*, 15 arom. CH); 106.7 (*s*, C(2)); 97.5 (*s*, C(5)); 41.2, 41.1 (2*q*, Me_2N). CI-MS (NH_3): 358 (5, $M^{+\cdot}$), 327 (10, $[M - Me_2N + NH_4]^+$), 314 (28, $[M - Me_2N]^+$), 178 (100).

Crystals suitable for the X-ray crystal-structure determination were grown from $CDCl_3$ by slow evaporation of the solvent.

6.2. (E/Z)-N,N-*Dimethyl*-N*'-(2,3-diphenylprop-2-enylidene)hydrazine* (**23**) *and* N,N-*Dimethyl*-N-*(2,5-diphenyl-2,5-dihydrothiazol-5-yl)amine* (**24**). To a soln. of freshly prepared **9** (*ca.* 5 mmol) in a mixture of hexane and AcOEt (300 ml, 10:1), a soln. of **3d** (*ca.* 6 mmol) in toluene (150 ml) was slowly added at r.t.. Purification of the crude mixture after 1 h by SC (hexane/AcOEt 10:1 to 3:1) and MPLC (hexane/AcOEt 90:5) afforded 3 almost pure compounds: 163 mg (13%) and 54 mg (5%), respectively, of the (*E*)- and (*Z*)-isomer of **23** (*i.e.* **23a** and **23b**)[9]) and 75 mg (5%) of one of the diastereoisomers of **24**.

Data of **23a**: Yellowish oil. IR: 3019*m*, 2950*m*, 2851*m*, 2824*m*, 2786*m*, 1626*m*, 1593*m*, 1551*s*, 1491*s*, 1469*s*, 1446*s*, 1266*s*, 1129*m*, 1077*m*, 1043v*s*, 896*m*, 862*m*, 760*s*, 750*s*, 698v*s*, 607*m*. ^{1}H-NMR: 7.96 (*s*, CH=N); 7.88–7.59 (*m*, 10 arom. H); 7.06 (*s*, CH=C); 3.24 (*s*, Me_2N). ^{13}C-NMR: 161.9 (*d*, CH=N); 141.2, 139.6, 137.5 (3*s*, 2 arom. C, 1 =C); 132.1, 130.2, 129.3, 127.8, 127.6, 127.2, 126.9 (7*d*, 10 arom. CH, 1 =CH); 42.6 (*q*, Me_2N). CI-MS (NH_3): 252 (20), 251 (100, $[M + 1]^+$), 210 (16, $[M - Me_2N_2 + NH_4]^+$), 209 (99, $[M - Me_2N_2 + NH_3]^+$).

Data of **23b**: Colorless oil. IR: 3055*m*, 3022*m*, 2951*m*, 2854*m*, 2784*m*, 1595*m*, 1553*s*, 1444*s*, 1361*m*, 1272*s*, 1133*s*, 1040v*s*, 918*m*, 897*m*, 849*m*, 778*m*, 756v*s*, 703v*s*, 632*m*, 601*s*. ^{1}H-NMR: 7.70–7.54 (*m*, 5 arom. H); 7.53 (*s*, CH=N); 7.46–7.39 (*m*, 3 arom. H); 7.29–7.26 (*m*, 2 arom. H); 7.06 (*s*, CH=C); 3.21 (*s*, Me_2N). ^{13}C-NMR: 140.2, 139.1, 138.1 (3*s*, 2 arom. C, 1 =C); 137.0 (*d*, CH=N); 129.9, 129.8, 129.4, 128.2, 127.8, 127.0, 126.5 (7*d*, 10 arom. CH, 1 =CH); 42.7 (*q*, Me_2N). CI-MS (NH_3): 252 (19), 251 (100, $[M + 1]^+$), 223 (11, $[M - Me_2N + NH_4]^+$).

Data of *trans*-**24**: Colorless crystals. M.p. 86–88°. IR: 3080*w*, 3058*m*, 3024*m*, 2986*m*, 2959*m*, 2897*w*, 2843*w*, 2816*s*, 2772*s*, 1655*s*, 1595*w*, 1580*w*, 1488*s*, 1469*m*, 1451v*s*, 1427*m*, 1253*m*, 1235*s*, 1154*m*, 1095*m*, 1082*m*, 1064*s*, 1042*m*, 1028*m*, 996v*s*, 979*s*, 943*m*,

[9]) It was not possible to assign the spectras to (*E*)- and (*Z*)-**23** on the basis of the present information.

923*s*, 911*s*, 857*m*, 844*s*, 780*w*, 754v*s*, 732v*s*, 695v*s*, 633v*s*, 613*s*. ^{1}H-NMR: 8.02–8.00 (*d*-like, 2 arom. H); 7.99–7.50 (*m*, 6 arom. H); 7.49 (*d*, *J* = 2.9, HC(4)); 7.48–7.37 (*m*, 2 arom. H); 6.79 (*d*, *J* = 2.9, HC(2)); 2.39 (*s*, Me_2N). ^{13}C-NMR: 165.7 (*d*, C(4)); 141.0, 140.4 (2*s*, 2 arom. C); 128.7, 128.5, 128.5, 128.2, 127.9, 126.7 (6*d*, 10 arom. CH); 106.7 (*s*, C(5)); 83.5 (*d*, HC(2)); 40.6 (*q*, Me_2N). CI-MS (NH_3): 283 (10, $[M + 1]^+$), 251 (12, $[M – S + 1]^+$), 238 (100, $[M – Me_2N]^+$), 178 (88, $[M – PhCN]^+$).

Crystals suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2/hexane by slow evaporation of the solvent.

7. *X-Ray Crystal-Structure Determination of* **17, 18**, **21**, and *trans*-**24** (*Table* and *Figs. 1-3*)[10]). All measurements were performed on a *Nonius KappaCCD* diffractometer [22] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. The data collection and refinement parameters are given in the *Table*, and views of the molecules are shown in *Figs. 1-3*. Data reduction was performed with *HKL Denzo* and *Scalepack* [23]. The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multi-scan method [24] was applied in the cases of **18** and *trans*-**24**. Equivalent reflections were merged with the exception of the *Friedel* pairs of **21**. The structures were solved by direct methods using SHELXS97 [25] (for **17**) and SIR92 [26] (for **18**, **21** and *trans*-**24**), which revealed the positions of all non-H-atoms. In the case of **21**, there are two symmetry-independent molecules in the asymmetric unit. The atomic coordinates of the two molecules were tested carefully for a relationship from a higher symmetry space group using the program *PLATON* [27], but none could be found. In addition, both molecules are disordered by inversion of each entire molecule about its centre of gravity. Refinement of constrained site occupation factors for the two orientations of each molecule yielded values of 0.934(1) and 0.935(1) for the major conformation of molecules A and B, respectively. An extensive series of similarity restraints was applied in order to keep the chemically equivalent bond lengths and angles about all atoms in the minor components to be similar to those of the major components. Furthermore, neighboring atoms within and between each disordered orientation were restrained to have similar atomic displacement parameters. The non-H-atoms of the major orientations were refined anisotropically, while those of the minor

[10]) CCDC-611000–611003 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Center via* http://www.ccdc.cam.ac.uk/data_request/cif.

orientations were refined isotropically. The non-H-atoms of **17**, **18**, and *trans*-**24** were refined anisotropically. The amine H-atom of **17** was placed in the position indicated by a difference electron density map and its position was allowed to refine together with an isotropic displacement parameter. All remaining H-atoms of **17** and all of the H-atoms of **18**, **21**, and *trans*-**24** were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for any Me group). The refinement of each structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. Corrections for secondary absorption were applied, except in the case of **18**. In **17**, **18**, **21**, and *trans*-**24**, 1, 3, 8, and 2 reflections, respectively, whose intensities were considered as extreme outliers, were omitted from the final refinement. Refinement of the absolute structure parameter [28] for **21** yielded a value of 0.45(4), which indicates that the structure is an inversion twin. For **17**, the space group permits the compound to be enantiomerically pure, but the absolute configuration could not be determined. The enantiomer used in the refinement model was chosen arbitrarily. Neutral atom scattering factors for non-H-atoms were taken from [29a], and the scattering factors for H-atoms were taken from [30]. Anomalous dispersion effects were included in F_c [31]; the values for f' and f'' were those of [29b]. The values of the mass attenuation coefficients are those of [29c]. All calculations were performed using the SHELXL97 [32] program.

Table. *Crystallographic Data of Compounds* **17**, **18**, **21**, *and* trans-**24**.

	17	**18**	**21**	*trans*-**24**
Crystallized from	CH_2Cl_2/ Pentane	hexane/AcOEt/ Et_2O	$CDCl_3$	CH_2Cl_2/hexane
Empirical formula	$C_{12}H_{18}N_2O_6$	$C_{23}H_{22}N_2$	$C_{23}H_{22}N_2S$	$C_{17}H_{18}N_2S$
Formula weight [g mol^{-1}]	286.28	326.44	358.5	282.4
Crystal color, habit	colorless, prism	colorless, prism	colorless, prism	colorless, prism
Crystal dimensions [mm]	0.22 × 0.25 × 0.32	0.10 × 0.15 × 0.22	0.10 × 0.15 × 0.25	0.20 × 0.22 × 0.30
Temperature [K]	160(1)	160(1)	160(1)	160(1)
Crystal system	orthorhombic	triclinic	monoclinic	monoclinic
Space group	$P2_12_12_1$	$P\bar{1}$	Cc	$P2_1/n$
Z	4	2	8	4
Reflections for cell determination	14502	4028	5653	34463
2θ range for cell determination [°]	4 – 55	4 – 55	4 – 60	4 – 60
Unit cell parameters a [Å]	7.8473(2)	9.9323(3)	12.9159 (1)	10.9672(2)
b [Å]	10.3424(2)	9.9977(3)	15.0573 (2)	6.0702(1)
c [Å]	17.3424(5)	10.4338(3)	20.1476 (2)	22.4345(4)
α [Å]	90	62.635(2)	90	90
β [°]	90	84.408(1)	106.6416(6)	91.248(1)
γ [Å]	90	78.997(1)	90	90
V [Å^3]	1407.51(6)	903.16(5)	3754.16(7)	1493.18(5)
D_x [g cm^{-3}]	1.351	1.200	1.268	1.256
μ(MoK_α) [mm^{-1}]	0.109	0.0703	0.181	0.208
Scan type	ϕ and ω	ϕ and ω	ω	ϕ and ω
$2\theta_{max}$ [°]	55	55	60	60
Transmission factors (min; max)	0.816; 0.925	–	–	0.870; 0.961
Total reflections measured	20739	21209	52142	38665
Symmetry-independent reflections	1867	4105	10265	4378
Reflections with $I > 2\sigma(I)$	1679	2953	8259	3218
Reflections used in refinement	1866	4102	10257	4376
Parameters refined; restraints	189; 0	229; 0	684; 1266	184; 0
R (on F; $I > 2\sigma(I)$ reflections)	0.0390	0.0483	0.0421	0.0449
wR (on F^2; all indept. reflections)	0.1050	0.1375	0.1000	0.1166
Weighting parameters [a, b][a]):	0.0578; 0.3696	0.0785; 0.0696	0.0506; 0.966	0.0533; 0.4053
Goodness of fit	1.066	1.045	1.024	1.062
Secondary extinction coefficient	0.032(6)	0.040(8)	-	0.069(4)
Final Δ_{max}/σ	0.001	0.001	0.001	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.28; -0.24	0.25; -0.22	0.24; -0.27	0.30; -0.27

[a]) $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$, where $P = (F_o^2 + 2F_c^2)/3$.

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Chapter 6

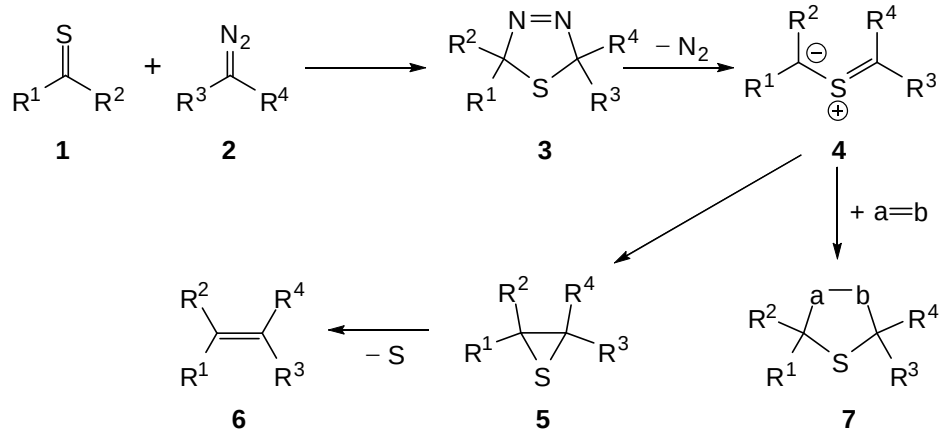
Reactions of Thioketones Possessing a Conjugated C=C Bond with Diazo Compounds [1])

The reactions of several thioketones containing a conjugated C,C-double bond with diazo compounds were investigated. All of the selected compounds reacted *via* a 1,3-dipolar cycloaddition with the C=S group and subsequent N_2-elimination to yield thiocarbonyl ylides as intermediates, which underwent a 1,3-dipolar electrocyclization to give the corresponding thiirane **25**, or, by a subsequent desulfurization, to give the olefins **33a, 33b**. None of the intermediate thiocarbonyl ylides reacted under inclusion of the conjugated C,C-double bond *via* 1,5-dipolar electrocyclization. If the α,β-unsaturated thiocarbonyl compound bears an amino group in β-position, the reactions with diazo compounds led to the 2,5-dihydrothiophenes **40a** – **40d**. In these cases, the proposed mechanism of the reactions led once more to the thiocarbonyl ylides **36** and thiiranes **38**, respectively. The thiiranes reacted *via* a S_Ni'-like mechanism to the corresponding thiolate/ammonium-zwitterion **39**, which underwent a ring closure to yield the 2,5-dihydrothiophenes **40**. Also in these cases, no 1,5-dipolar electrocyclization could be observed. The structures of several key products were established by X-ray crystallography.

1. Introduction. – The reactions of thiocarbonyl compounds **1** with diazo compounds have been investigated extensively (*e.g.* [1-3], for reviews see [4][5]). The reactions proceed *via* a 1,3-dipolar cycloaddition to give the five-membered 2,5-dihydro-1,3,4-thiadiazoles **3**, which, in general, at room temperature eliminate N_2 in a cycloreversion, leading to a thiocarbonyl ylide **4** (*Scheme 1*). In the absence of dipolarophiles, the thiocarbonyl ylides **4** react in a 1,3-dipolar electrocyclization to give the thiiranes **5**, which, either spontaneously or by treatment with Ph_3P, undergo a desulfurization to yield the olefins **6**. In the presence of appropriate dipolarophiles, *e.g.* an excess of the thiocarbonyl compound **1** [6][7], the thiocarbonyl ylides **4** can be intercepted to give five-membered heterocycles of type **7** formed in a 1,3-dipolar cycloaddition (*Scheme 1*).

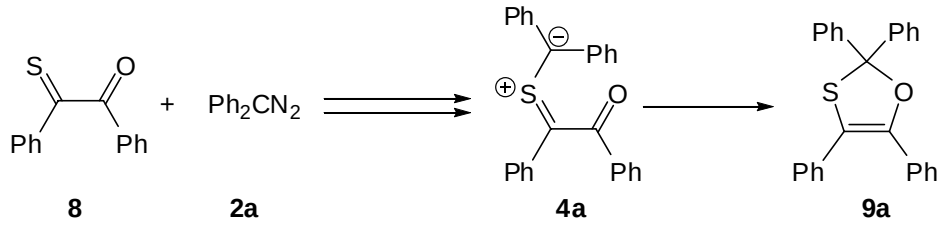
[1]) D. H. Egli, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2006**, *89*, 3041.

Scheme 1



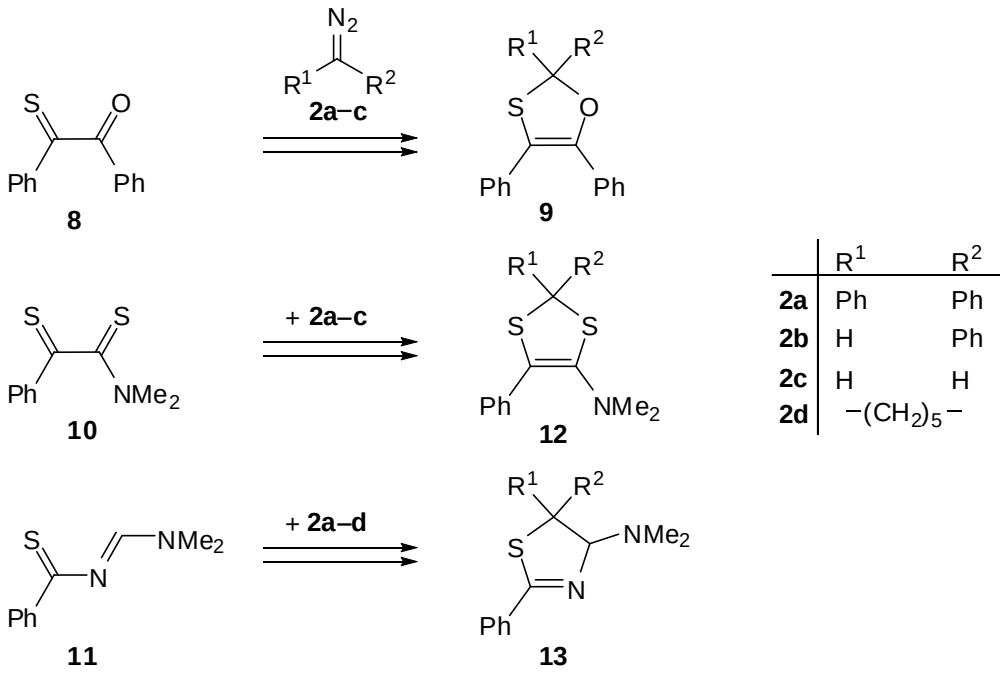
In 1979, *Bak* and *Praefcke* have shown that the reaction of 1,2-diphenyl-2-thioxoethanone (**8**) with diphenyldiazomethane (**2a**) yields the corresponding 1,3-oxathiole **9a**, which is formed by a 1,5-dipolar electrocyclization of the intermediate thiocarbonyl ylide **4a** under incorporation of the C=O bond [8] (*Scheme 2*). Analogous products have been obtained from thioketones and α-diazo carbonyl compounds [9 – 11].

Scheme 2



Recently, we have investigated reactions of diazo compounds with thiocarbonyl compounds containing a conjugated π-system, such as α-thioxoketones, α-thioxothioamides, etc. Since the reactions of **8**, *N,N*-dimethyl-2-phenyl-2-thioxothioacetamide (**9a**), and *N*-[(dimethylamino)methylene]thiobenzamide (**11**) with different diazo compounds led to the five-membered heterocycles **9**, **12** and **13**, respectively, usually in good yields [12][13] (*Scheme 3*), we decided to investigate whether the analogous reaction takes place with α,β-unsaturated thioketones, *i.e.* when the conjugated π-system is a C,C-double bond.

Scheme 3

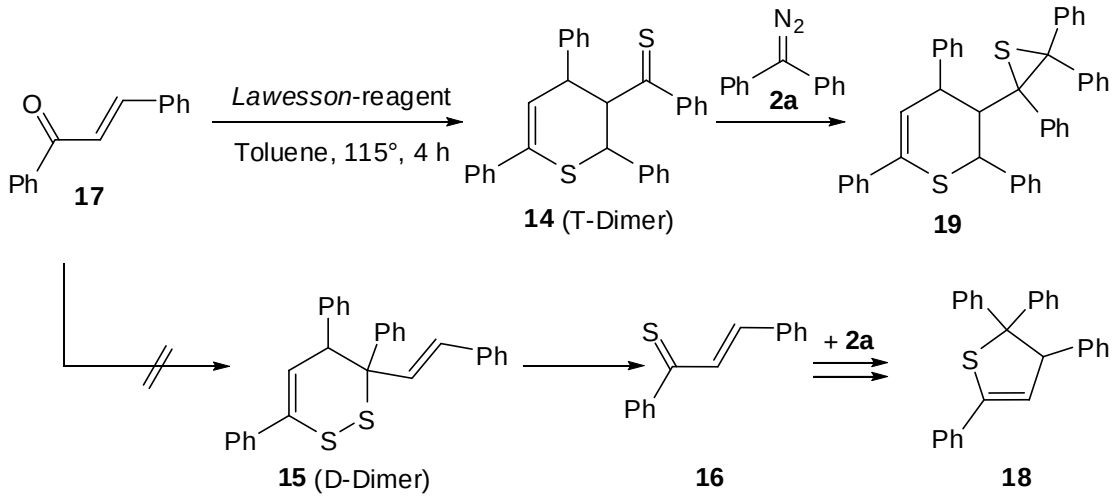


The synthesis of such α,β-conjugated thioketones proved to be no trivial task, because these products tend to dimerize in a [2 + 4]-cycloaddition. In a few cases it was possible to prepare the desired synthon and to let it react with diphenyldiazomethane (**2a**). In order to make the thioketone less vulnerable to dimerization and to be able to carry out reactions with different diazo components, we extended the study to α,β-unsaturated thioketones with a β-amino substituent, *i.e.*, to vinylogous thioamides.

2. Results and Discussion. – 2.1. *Reaction with (Phenyl)(3,4-dihydro-2,4,6-triphenyl-2*H*-thiopyran-3-yl)methanethione* (**14**). It was attempted at first to synthesize the 'D-dimer' **15** of thiachalcone **16** by thionation of chalcone **17** [14]. The dimer would then be subjected to a retro-*Diels-Alder* reaction in the presence of diphenyldiazomethane (**2a**), which should lead to 2,3,5,5-tetraphenyl-2,3-dihydrothiophene (**18**) *via* 1,5-dipolar electrocyclization of the intermediate thiocarbonyl ylide with an extended π-system. Unfortunately, as reported by *Li et al*. [15], we were unable to reproduce the results of *Saito et al*. [14] and failed to isolate **15**. The only product obtained after thionation of **17** was the so-called 'T-Dimer' **14** [15]. Although **14** is less suitable as a precursor of **16** than **15**, we tried to carry out the reaction with **2a**. A reaction temperature of 50° to 60° and slow addition of the diazo compound to the solution of **14** in benzene were chosen as the reaction condition to make a retro-*Diels-Alder* reaction possible. But **14** reacted with **2a** at

the C=S group before the retro-*Diels-Alder* reaction took place to give thiirane **19** (*Scheme 4*). The structure of **19** has been elucidated by an X-ray crystal-structure determination (*Fig. 1*). The asymmetric unit contains one molecule of **19** plus one half of a H_2O molecule disordered across two sites. The six-membered thiopyrane ring shows a half-chair conformation twisted on C(2)-C(3) and the phenyl substituents at C(4) and C(7) are almost coplanar. Surprisingly, **19** could not be desulfurized with Ph_3P to yield the corresponding alkene, most likely because the S-atom is too much hindered for an attack of Ph_3P. *Fig. 1* shows that the S-atom of the thiirane is indeed sheltered from a nucleophilic attack.

Scheme 4



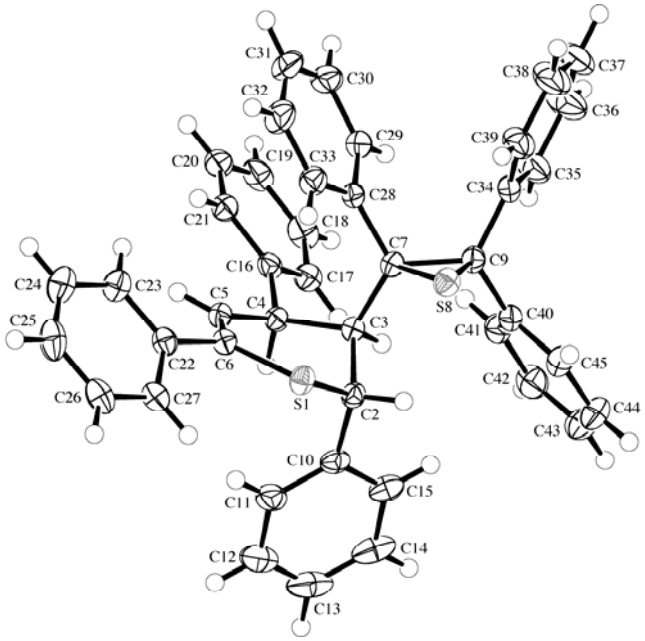
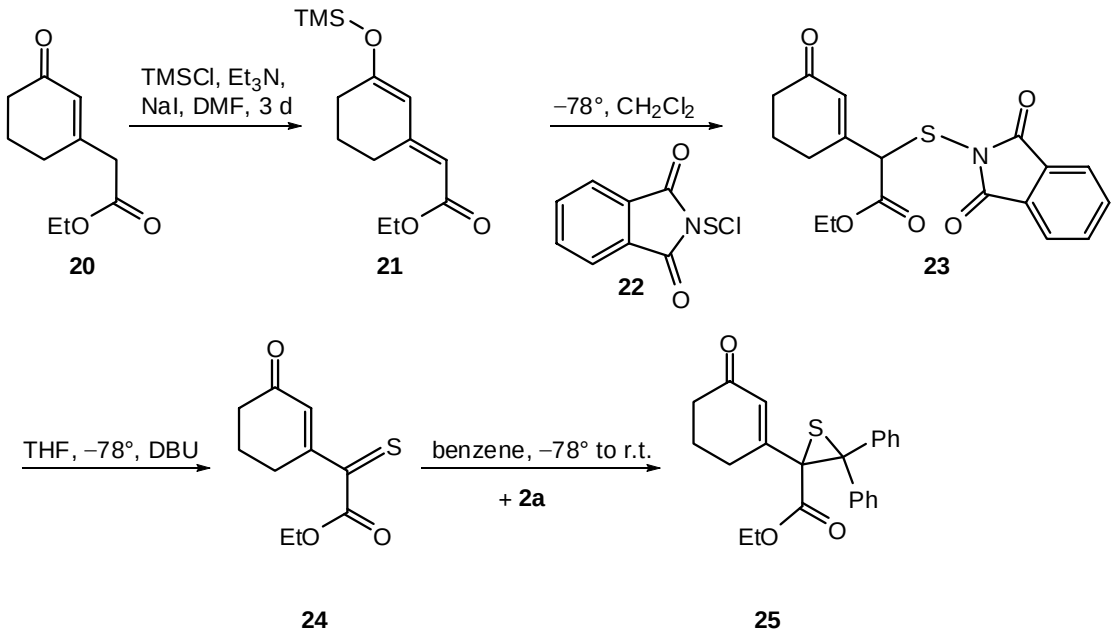


Fig. 1 *ORTEP Plot* [16] *of the molecular structure of* **19** (50% probability ellipsoids, arbitrary numbering of the atoms)

2.2. *Reactions with γ-Oxo-α,β-unsaturated thioketones*. As α,β-unsaturated thioketones are prone to dimerize *via* [2 + 4] cycloaddition, the preparation of these synthons need special reaction conditions. One possibility is to create the thiocarbonyl group in the last step, *e.g.*, by a base catalyzed reaction at low temperature. The ethyl acetate **20** was synthesized according to a procedure described by *Mc Murry et al.* [17]. Silylation of **20** was achieved at room temperature by using NaI as a catalyst in equimolar ratio to give the silylenolether **21**, which was converted into **23** by using sulfenylchloride **22** at –78° in CH_2Cl_2 (*Scheme 5*). The addition of **22** in 2-position of silylenolethers of type **21** was never observed in such reactions (see also the reaction of **30a**,**b** with **22**, *Scheme 7*). Then, the thioketone **24** was generated *in situ* by DBU-catalyzed elimination at low temperature and used immediately for the reaction with **2a**. After chromatographic work up, thiirane **25** was obtained in 30% yield as a brownish oil.

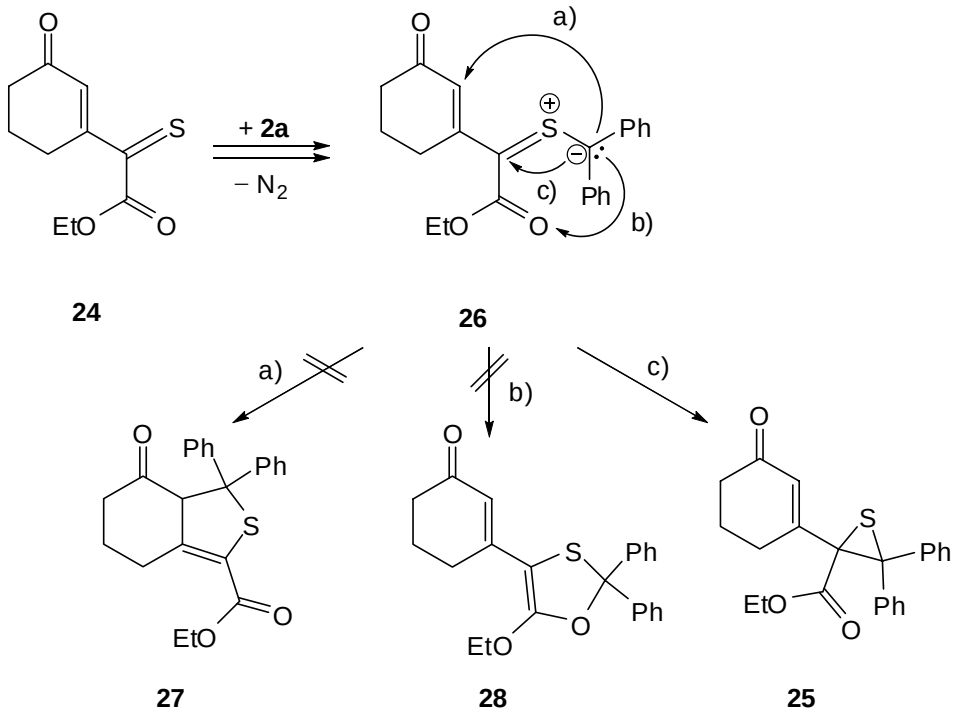
Scheme 5



A mechanistic interpretation of the reaction is shown in *Scheme 6*. The reaction of **24** with **2a** led to the intermediate thiocarbonyl ylide **26** which could react to give stable products *via* three different pathways. Reactions a) and b), *i.e.* 1,5-dipolar electrocyclizations *via* the conjugated C=C or C=O bond, respectively, could yield either thiophene **27** or 1,3-oxathiole **28**. The third pathway c) would lead to thiirane **25** by a 1,3-dipolar electrocyclization. The spectroscopic data of the isolated product (IR: three intensive absorptions at 1741 (CO_2Et), 1714 (CO), and 1642 cm^{-1} (C=C); ^{13}C-NMR: 199.2 (CO),

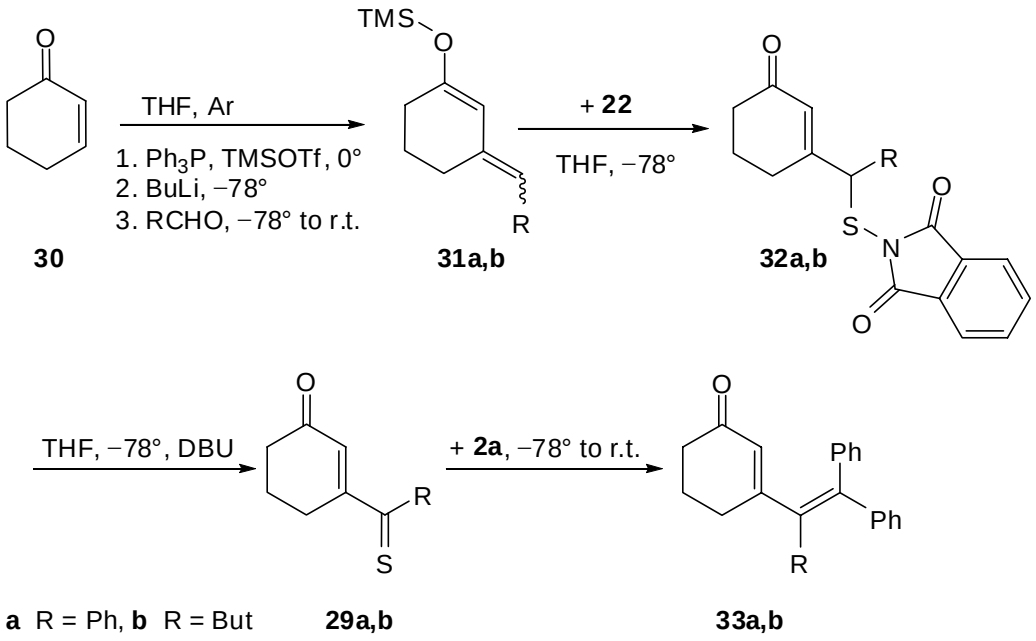
167.3 (CO_2Et), 158.7 (*s*) and a *d* between 132.1 and 127.7 ppm (C=CH)) show clearly that it was neither the expected dihydrothiophene **27**, nor the 1,3-oxathiole **28**, but the thiirane **25**.

Scheme 6



Two other α,β-unsaturated thioketones **29a** and **29b** have been prepared as depicted in *Scheme 7*. In a *Wittig*-like reaction of cyclohex-2-enone (**30**) with benzaldehyde and pentanal, respectively, using the method of *Kozikowski* and *Jung* [18], the silylenolethers **31a** and **31b** were obtained. In the following steps, the protocol of *Capozzi et al.* was applied [19]. Treatment of **31** with **22** in THF at –78° gave the isoindole derivatives **32** in about 70% yield with a significant amount of the corresponding ketones of the hydrolyzed silylenolethers **31**. The crude products **32** in THF were treated with DBU at –78° leading to the thioketones **29** by elimination of phthalimide. The crude **29a** and **29b**, respectively, were reacted with **2a** to give the alkenes **33a** and **33b** (*Scheme 7*). None of the expected intermediate thiiranes could be detected, but they spontaneously underwent desulfurization.

Scheme 7



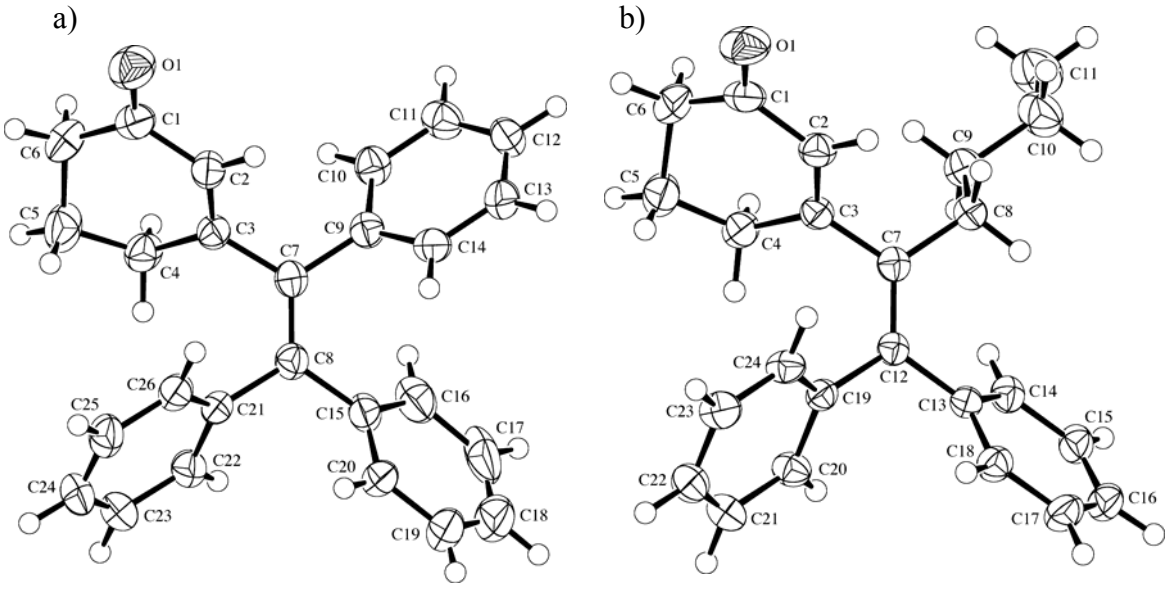


Fig. 2 *ORTEP Plot* [16] *of the molecular structure of a)* **33a** *and b)* **33b** (50% probability ellipsoids, arbitrary numbering of the atoms)

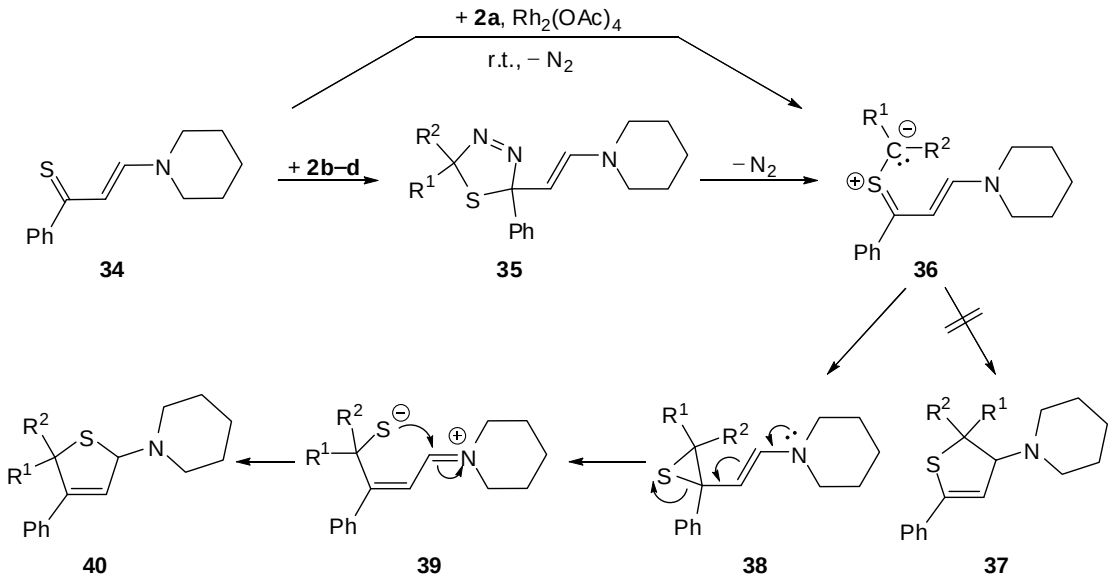
The structures of **33a** and **33b** have been established by X-ray crystallography (*Fig. 2*). Both structures are, with the exception of the substituent at C(7), quite similar. The conjugated π-system from O(1) to C(8), including C(1), C(2), C(3), and C(7) is twisted about C(3)–C(7) (torsion angle C(2)–C(3)–C(7)–C(8) 131.5(3)° and C(2)–C(3)–C(7)–C(12) 124.5(2)°, resp.). All phenyl substituents in compound **33a** are, because of steric

reasons, twisted out of the plane formed by C(3), C(7) and C(8) (torsion angles C(7)–C(8)–C(21)–C(22) 126.6(3)°, C(7)–C(8)–C(15)–C(16) –47.0(5)°, and C(8)–C(7)–C(9)–C(10) 134.2(3)°). The situation in **33b** is almost the same as in **33a** with the exception of the butyl-substituent at C(7), which is in the expected staggered form.

The reactions of **2a** with the α,β-unsaturated thioketones **24**, **29a** and **29b** show that these conjugated thiocarbonyl compounds, which do not possess a heteroatom as part of the conjugated system, react readily with diazo compounds to give thiocarbonyl ylides as reactive intermediates. But in contrast to thiocarbonyl ylides bearing conjugated C=O, C=S or C=N groups, these intermediates do not undergo a 1,5-dipolar electrocyclization. The products obtained, namely the alkenes **33a** and **33b** and the thiirane **25** are the result of a 1,3-electrocyclization.

2.3. Reactions with (E)*-1-Phenyl-3-piperidinoprop-2-ene-1-thione* (**34**) [20]. The α,β-unsaturated thioketone **34** reacted with **2a** much slower than other thioketones [12][13]. Normally, the reaction between thioketones and diazo compounds are complete in a few min or h, while in the case of **34** the reactions needed several days at 40-80°. Nevertheless, the results were satisfactory as all spectra (MS, ^{1}H-, ^{13}C-NMR, IR) indicated the presence of dihydrothiophenes as the main products. In the case of **2a**, the reaction had to be catalyzed by $Rh_2(OAc)_4$. After 4 h at room temperature, a dihydro(triphenyl)(piperidino)-thiophene was obtained in 50% yield. Analogous products were isolated in relatively good yields when **34** was treated with diazo compounds **2b**, **2c,** and diazocyclohexane (**2d**), respectively, under thermal conditions. In two cases, *i.e.* with **2b** and **2c**, we were able to grow single-crystals of the resulting products, which were suitable for an X-ray structure determination (*Fig. 3*). Surprisingly, the products were not the expected 4,5-dihydrothiophenes **37** which should be formed *via* 1,5-dipolar electrocyclization of the intermediate thiocarbonyl ylide **36**, but 2,5-dihydrothiophenes of type **40** (*Scheme 8*). Apparently, the S-atom is in a different position in the ring. A likely mechanistic explanation is given in *Scheme 8*: instead of the expected 1,5 dipolar electrocyclization of thiocarbonyl ylide **36** to give **37**, **36** reacted in a 1,3-dipolar electrocyclization to yield thiirane **38**. The latter underwent a ring opening in a S_Ni'-like reaction supported by the free electron pair of the N-atom to give the zwitterion **39**, which underwent a 5-*exo*-*trig* cyclization, leading to **40**.

Scheme 8



Whereas the reaction of **34** with **2c** yielded **40c** as the only product, the reaction with **2b** resulted in two diastereoisomeric products (*cis*-**40b** and *trans*-**40b**), which could be separated by MPLC. Recrystallization of the *cis*-isomer gave crystals suitable for X-ray crystallography (*Fig. 3*). The data of the second isomer are in accordance with the estimated values for *trans*-**40b'**.

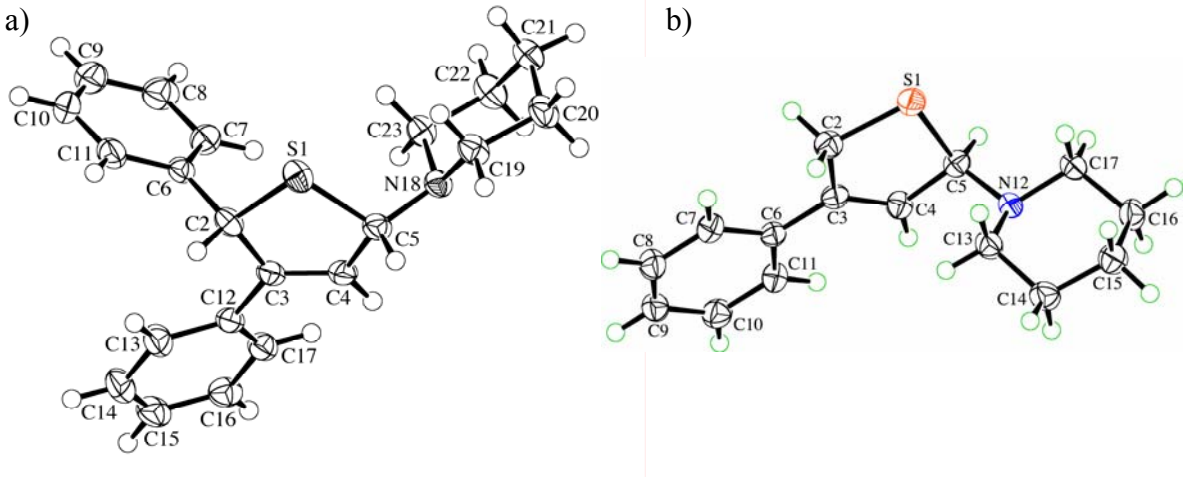


Fig. 3 *ORTEP Plot* [16] *of the molecular structure of a) cis*-**40b** *and b)* **40c** (50% probability ellipsoids, arbitrary numbering of the atoms)

3. Conclusion. – The results in the present work show that it is possible to prepare the *α,β*-unsaturated thioketones **24**, **29a**, and **29b** *in situ* by a base catalyzed reaction at low temperature. The products of their reactions with diphenyldiazomethane (**2a**) indicate that thiocarbonyl ylides (*i.e.* **26**, *Scheme 6*) are formed as intermediates, which react in a 1,3-dipolar electrocyclization to give the corresponding thiiranes (*i.e.* **25**), but they do not undergo the expected 1,5-dipolar electrocyclization.

In the case of **34** with an amino group in *β*-position, diazo compounds **2b** – **2d** react also in a 1,3-dipolar cycloaddition onto the C=S group to give the 2,5-dihydro-1,3,4-thiadiazoles **35** as intermediates, followed by a spontaneous cycloreversion, which leads to the thiocarbonyl ylides **36**. A subsequent 1,3-dipolar electrocyclization yields the thiiranes **38**, which further rearrange to give finally the 2,5-dihydrothiophenes **40a** – **40d**. In all of the investigated reactions of *α,β*-unsaturated thioketones there was no 1,5-dipolar electrocyclization observed.

We thank the analytical units of our institute for spectra and analyses, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for financial support.

Experimental Part

1. *General.* See [12][13].

2. *Starting Materials.* All thiocarbonyl derivatives and their precursors and all diazo compounds were prepared following known protocols: (phenyl)(3,4-dihydro-2,4,6-triphenyl-2*H*-thiopyran-3-yl)methanethione (**14**) [14], diphenyldiazomethane (**2a**) [8], phenyldiazomethane (**2b**) [21], diazomethane (**2c**) [22], diazocyclohexane (**2d**) [23], ethyl(3-oxocyclohex-1-en-1-yl)acetate (**20**) [17], 1,3-dihydro-1,3-dioxo-2*H*-isoindole-2-sulfenylchloride (**22**) [24], (*E*)-1-phenyl-3-piperidinoprop-2-ene-1-thione (**34**) [20]. All other reagents are commercially available.

3. *General Procedure A* (*GP A*): A stirred soln. of the precursor of the thiocarbonyl compound (2–6 mmol) in THF (50–100 ml) was cooled to –78° and DBU was added drop-wise by means of a syringe. The color of the soln. changed rapidly. After a few min, a purple soln. of **2a** in benzene (10–25 ml, 3–7 mmol) was added slowly and N_2 evolved. The color of the soln. changed again and the mixture was allowed to warm to r.t. The solvent was removed, and the crude product was purified by chromatography.

4. *General Procedure B* (*GP B*): To a soln. of the thiocarbonyl compound (1–7 mmol) in CH_2Cl_2 (30–100 ml), the diazo compound (2–8 mmol) in toluene, Et_2O, THF or benzene (30–130 ml) was added by means of a dropping funnel, or, in the case of **2c,** by means of a *Pasteur* pipette. After total conversion of the thiocarbonyl compound, monitored either by TLC (treated for 20 s with a soln. of 1% Et_3N in Et_2O), color change or evolution of N_2[2]), the solvent was evaporated and the mixture was purified by chromatography using silica gel, which had been treated with 3% Et_3N. Furthermore, the solvent was doped with 1% of Et_3N.

5. *Reaction of (Phenyl)(3,4-dihydro-2,4,6-triphenyl-2*H*-thiopyran-3-yl)methanethione* (**14**) *with* **2a**. A soln. of **14** (2 mmol) in benzene (20 ml) was heated to 50° and **2a** (*ca.* 5 mmol) in benzene (10 ml) was added slowly. After total conversion of the starting material (TLC, changing of the color of the soln. from blue to yellow-brown), the solvent was evaporated, the crude product was purified by CC (hexane/AcOEt 10:1), and recrystallized from CH_2Cl_2/hexane: 313 mg (51%) of *3,4-dihydro-2,4,6-triphenyl-3-(2,3,3-triphenylthiiran-2-yl)-2*H*-thiopyrane* (**19**). Yellowish crystals. M.p. 137–141°. IR: 3054*m*, 3024*m*, 2932*w*, 1598*m*, 1491v*s*, 1444*s*, 1267*w*, 1235*w*, 1180*w*, 1156*w*, 1077*w*, 1031*m*, 1001*w*, 778*m*, 751v*s*, 696v*s*. ^{1}H-NMR: 7.75 (*d*, *J* = 6.9, 2 arom. H); 7.61 (*d*, *J* = 6.9, 2 arom. H); 7.56–6.45 (*m*, 26 arom. H); 6.12 (*d*, *J* = 4.0, =CH); 4.32 (*d*-like, H-C(2)); 3.71 (*t*-like, H-C(4)); 3.55 (br. *s*, H-C(3)). ^{13}C-NMR: 142.0, 139.9, 139.8, 137.2 134.3, 133.4 (6*s*, 6 arom. C); 132.0, 130.3, 128.5, 128.4, 128.1, 128.0, 127.8, 127.0, 126.7, 126.5, 126.1, 126.0, 125.9, 125.4 (14*d*, 30 arom. CH); 120.3 (*d*, =CH); 65.3, 64.7 (2*s*, 2 C(2'), C(3')); 52.3 (*d*, C(2)); 47.9 (*d*, C(4)); 39.4 (*d*, C(3)). CI-MS (*i*-butane): 391 (42, $[M + 1 - C_{15}H_{12}S)]^+$), 358 (100, $[M - C_{15}H_{12}S_2]^{+\cdot}$), 225 (100, $[C_{15}H_{12}S]^{+\cdot}$). Anal. calc. for $C_{43}H_{34}S_2 \cdot ½H_2O$ (623.883): C 82.79, H 5.66, S 10.28; found: C 83.44, H 5.65, S 9.96.

Crystals suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2 by slow evaporation of the solvent.

[2]) The evolution of N_2 was determined volumetrically using a gas burette attached to the reaction vessel.

6. *Reaction of Ethyl 2-(3-Oxocyclohexen-1-yl)-2-thioxoacetate* (**24**) *with* **2a**.

6.1. *Ethyl* (E/Z)-*2-{3-[(Trimethylsilyl)oxy]cyclohex-2-en-1-yliden}acetate* (**21**). To a soln. of **20** (2 g, 10.98 mmol) and Me_3SiCl (1.63 g, 15 mmol) in DMF (15 ml), Et_3N (1.52 g, 15 mmol) was added slowly (10 min) whereby a white precipitate was formed. After a few min, NaI (1.8 g, 12 mmol) was added in one portion, and the mixture was stirred for 3 d at r.t. Pentane (30 ml) was added, and the resulting suspension was stirred for 1 h to give a better treatable precipitation. The soln. was filtered and the solvent was removed *i.v.*. The residue was once more suspended in pentane (20 ml) and filtered to give **21** as a mixture of the (*E*/*Z*)-isomers: 2.54 g (96%). Pale yellowish oil. ^{1}H-NMR (major product)[3]): 6.95 (*s*, HC(2)); 5.22 (*s*, HC(2')); 4.11–4.04 (*m*, CH_2O); 2.26–2.21 (*m*, $H_2C(6')$); 2.18–2.13 (*m*, $H_2C(4')$); 1.75–1.70 (*m*, $H_2C(5')$); 1.22–1.17 (*m*, *Me*CH_2); 0.24 (*s*, Me_3Si); (minor product): 5.38 (*s*, HC(2)); 5.34 (*s*, HC(2')); 0.18 (*s*, Me_3Si)[4]). ^{13}C-NMR (major product): 166.9 (*s*, CO_2); 163.4 (*s*, C(1')); 154.7 (*s*, C(3')); 109.6, 105.3 (2*d*, C(2), C(2')); 58.9 (*t*, CH_2O), 31.7 (*t*, C(6')); 30.8 (*t*, C(4')); 22.2 (*t*, C(5')); 14.3 (*q*, *Me*CH_2); 0.0 (*q*, (Me_3Si); (minor product): 167.2 (*s*, CO_2); 162.5 (*s*, C(1')); 156.4 (*s*, C(3')); 107.5 (*d*, C(2) or C(2')); 58.9 (*t*, CH_2O), 30.5 (*t*, C(6')); 25.4 (*t*, C(4')); 22.0 (*t*, C(5')); 14.3 (*q*, *Me*CH_2); 0.1 (*q*, (Me_3Si).

6.2. *Ethyl 2-[(1,3-Dihydro-1,3-dioxo-2*H*-isoindol-2-yl)sulfanyl]-2-(3-oxocyclohexen-1-yl)acetate* (**23**). A soln. of **21** (0.50 g, 2.1 mmol) in dry CH_2Cl_2 (40ml) was cooled to –78°, and a soln. of **22** (0.47g, 2.2 mmol) in dry CH_2Cl_2 (*ca*. 20 ml) was added within 10 min by means of a syringe. The soln. was allowed to warm to r.t., the solvent was removed and the crude product was dried (h.v.) and analyzed without further purification: 0.69 g (100%) **23** (containing small amounts of **20**). ^{1}H-NMR: 7.91–7.84 (*m*, 2 arom. H); 7.81–7.29 (*m*, 2 arom. H); 5.71 (*s*, HC(2')); 4.67 (*s*, HC(2)); 4.27 (2*q*, *J* = 7.1, CH_2O); 2.42–2.32 (*m*, $H_2C(4')$, $H_2C(6')$); 2.11–2.05 (*m*, $H_2C(5')$); 1.31 (*t*, *J* = 7.1, Me). ^{13}C-NMR: 198.6 (*s*, C=O); 167.5 (*s*, $N(CO)_2$); 166.3 (*s*, =C(1')); 155.3 (*s*, CO_2Et); 134.9, 124.0 (2*d*, 4 arom. CH); 131.5 (*s*, 2 arom. C); 130.0 (*d*, C(2')); 62.7 (*t*, CH_2O); 59.5 (*d*, C(2)); 37.1 (*t*, $H_2C(4')$); 25.4 (*t*, $H_2C(6')$); 22.2 (*t*, $H_2C(5')$); 13.9 (*q*, Me).

[3]) It was not possible to assign the spectra to (*E*)- and (*Z*)-**21** on the basis of the present information. Due to thermodynamic stability, we expect that the minor product is the (*Z*)-isomer.

[4]) Other signals overlap with the corresponding signals of the major product.

6.3. Ethyl 2-(3-Oxocyclohexen-1-yl)-3,3-diphenylthiirane-2-carboxylate (**25**). According to *GP A,* a soln. of **23** (3.1 mmol) in CH_2Cl_2 (30 ml) was treated with a catalytic amount of DBU. After 30 min, an excess of **2a** (*ca.* 5 mmol) dissolved in benzene (20 ml) was added drop-wise. The mixture was diluted with 40 ml of CH_2Cl_2 and extracted with cold, sat. *aq.* NH_4Cl. The org. layer was dried (Na_2SO_4) and the solvent removed. CC (CH_2Cl_2/Et_2O 200:1): 344 mg (30%) of **25**. Brownish oil. IR: 3058*w*, 3027*w*, 2942*m*, 1741v*s*, 1714v*s*, 1642v*s*, 1623*m*, 1491*m*, 1445*s*, 1341*m*, 1324*m*, 1298*m*, 1241v*s*, 1187*s*, 1135*m*, 1094*m*, 1018*m*, 974*w*, 754*m*, 703v*s*. ^{1}H-NMR: 7.50–7.18 (*m*, 10 arom. H); 6.30 (*s*, =CH); 3.95–3.83 (*m*, CH_2O); 2.58 (*ddd*, *J* = 17.8, 2.7, 1.7, 1 H of $H_2C(6')$); 2.30–2.10 (*m*, $H_2C(4')$); 1.97 (*ddd*, *J* = 17.8, 4.3, 0.9, 1 H of $H_2C(6')$); 1.76–1.65, 1.31–1.19 (2*m*, $H_2C(5')$); 0.91 (*t*, *J* = 7.1, Me). ^{13}C-NMR: 199.2 (*s*, CO); 167.3 (*s*, CO_2Et); 158.7 (*s*, C(1')); 139.5, 137.4 (2*s*, 2 arom. C); 132.1, 129.8, 129.6, 127.9, 127.8, 127.8, 127.7 (7*d*, 10 arom. C, =CH); 77.3 (*s*, C(3)); 62.7 (*s*, C(2)); 62.3 (*t*, CH_2O); 37.3 (*t*, C(4')); 30.7 (*t*, C(6')); 22.7 (*t*, C(5')); 13.5 (*q*, Me). CI-MS: 396 (5, $[M + NH_4]^+$), 379 (54, $[M + 1]^+$), 364 (5), 347 (100, $[M + 1 - S]^+$).

7. *Reactions of (3-Oxocyclohexen-1-yl)(phenyl)methanethione* (**29a**) *and 1-(3-Oxocyclohexene-1-yl)pentanethione* (**29b**) *with* **2a**.

7.1. (E/Z)-*3-{3-[Trimethylsilyl)oxy]cyclohex-2-en-1-ylidene}methyl)benzene* (**31a**). To a cold (0°) soln. of cyclohex-2-enone (**30**) (2.06 g, 21.44 mmol) and Ph_3P (5.62 g, 21.44 mmol) in dry THF (50 ml) was added slowly TMSOTf (4.15 ml, 21.44 mmol). The mixture was cooled to –78°, and a soln. of BuLi (2.5 M in hexane, 8.4 ml, 21.44 mmol) was added slowly whereby the soln. changed to a dark brown suspension. Then, benzaldehyde (2.17 ml, 21.44 mmol) was added whereon the color turned to pale-orange. The solvent was removed and the residue was purified by "Kugelrohr"-destillation (115°, 5 mbar): 3.53 g (64%) of almost pure **31a**. Colorless oil. ^{1}H-NMR: 7.12–7.02, 6.97–6.93 (2*m*, 5 arom. H); 5.88, 5.82, 5.81, 5.37 (4*s*, HC(2), PhC*H*)[5]); 2.38–2.33, 2.17–2.12 (2*m*, $H_2C(4)$); 2.04–1.97 (*m*, $H_2C(6)$); 1.66–1.61, 1.57–1.52 (2*m*, $H_2C(5)$); 0.01 (*s*, Me_3Si). GC-MS (EI): 258 (100, $M^{+\cdot}$).

[5]) The product is a mixture of two stereoisomers (*E/Z*), therefore, four signals for the two olefinic H-atoms are to be expected. The assignment of the signals to HC(2) and PhC*H* is not clear.

7.2. (E/Z)-*3-Pentylidene-1-[(trimethylsilyl)oxy]cyclohexene* (**31b**). To a cold (0°) soln. of cyclohex-2-enone (**30**) (1.92 g, 20 mmol) and Ph_3P (5.25 g, 20 mmol) in dry THF (60 ml) was added slowly TMSOTf (4.76 g, 20 mmol). The soln. was cooled to –78°, and a soln. of BuLi (1.6 M in hexane, 13 ml, 20 mmol) was added slowly whereby the soln. changed to a dark brown suspension. Then, pentanal (1.72 ml, 20 mmol) was added by means of a syringe, and the color turned to orange. A part of the solvent was removed and the suspension was filtered. Then, the solvent was removed completely and the residue was purified by "Kugelrohr"-destillation (80–120°, 0.2 mbar): 1.53 g (32%) of almost pure **31b**. Colorless oil. ^{1}H-NMR: 5.32 (*s*, HC(2)); 4.95 (*t*-like, HC(1')); 2.17–2.13 (*m*, $H_2C(6)$); 2.12–2.10 (*m*, $H_2C(4)$); 2.05–1.97 (*m*, $H_2C(2')$); 1.70–1.63 (*m*, $H_2C(5)$); 1.29–1.24 (*m*, $H_2C(3')$, $H_2C(4')$); 0.85–0.80 (*m*, Me); 0.14 (*s*, Me_3Si). ^{13}C-NMR: 153.9 (*s*, C(1)); 134.2 (*s*, C(3)); 122.2 (*d*, C(2)); 110.4 (*d*, C(1')); 31.8 (*t*, C(6)); 30.2 (*t*, C(4)); 27.0 (*t*, C(2')); 24.1 (*t*, C(5)); 22.3 (*t*, C(3')); 22.0 (*t*, C(4')); 13.6 (*q*, C(5')); 0.0 (*q*, Me_3Si).

7.3. *2-{[(3-Oxocyclohexen-1-yl)(phenyl)methyl]sulfanyl}-1*H-*isoindole-1,3-(2*H*)-dione* (**32a**). A soln. of **31a** (1.01 g, 3.90 mmol) in dry THF (40 ml) was cooled to –78° and a soln. of **22** (0.71g, 3.90 mmol) in dry THF (*ca*. 25 ml) was added by means of a dropping funnel (30 min). The soln. was allowed to warm to r.t., the solvent was removed, and the crude product was dried (h.v.) and analyzed without further purifications: 1.27 g (89%) of **32a**[6]). Yellowish plates. IR: 2954*s*, 2871*m*, 1784*s*, 1738v*s*, 1704v*s*, 1666v*s*, 1495*m*, 1454*m*, 1340*m*, 1279v*s*, 1037v*s*, 968*m*, 866*s*, 763*m*, 710v*s*. ^{1}H-NMR: 7.87–7.76 (*AA*'BB', 2 arom. H); 7.74–7.66 (AA'*BB*', 2 arom. H); 7.38–7.14 (*m*, 4 arom. H); 7.10–7.07 (*m*, 1 arom. H); 5.80 (*t*, *J* = 1.3[7]), *H*CPh); 5.18 (*s*, HC(2')); 2.31–2.06 (*m*, $H_2C(4')$, $H_2C(6')$); 1.92–1.75 (*m*, $H_2C(5')$). ^{13}C-NMR: 199.1 (*s*, CO); 167.6 (*s*, $N(CO)_2$); 160.6 (*s*, =C); 136.9 (*d*, 1 arom. C); 134.7, 123.8 (2*d*, 4 arom. CH); 131.5 (*s*, 2 arom. C); 129.0, 128.9, 128.7, 128.3 (4*d*, 5 arom. CH, C(2')); 60.7 (*d*, *C*HPh); 37.2 (*t*, $H_2C(4')$); 29.1 (*t*, $H_2C(6')$); 25.8 (*t*, $H_2C(5)$). GC-MS (EI): 220 (30), 205 (100), 177 (30), 133 (15).

[6]) The NMR- and MS-spectra indicated a large amount of side product, which was formed by hydrolysis of **31a**.

[7]) The coupling constant of 1.3 Hz is also observed in one pair of signals in the *m* of $H_2C(6)$.

7.4. *2-{[(1-Oxocyclohexen-1-yl)pentyl]sulfanyl}-1*H-*isoindole-1,3(2*H*)-dione* (**32b**). A soln. of **31b** (1.44 g, 6 mmol) in dry THF (100 ml) was cooled to –78° and a soln. of **22** (1.28 g, 6 mmol) in dry THF (*ca*. 40 ml) was added by means of a dropping funnel (30 min). The soln. was allowed to warm to r.t., the solvent was then removed, and the crude product was dried (h.v.) and analyzed without further purifications: 1.97 g (92%) of **32b**. Yellowish oil. ^{1}H-NMR: 7.90–7.83, 7.79–7.71 (2*m*, 4 arom. H); 5.54 (s, HC(2')); 3.84–3.72 (*dd*, *J* = 6.4, 6.2, HC(1'')); 2.40–2.29 (*m*, H_2C(4')); 2.09–1.98 (*m*, H_2C(6')); 1.76–1.60 (*m*, H_2C(5')); 1.50–1.29 (*m*, H_2C(2''), H_2C(3''), H_2C(4'')); 0.94–0.90 (*m*, Me). ^{13}C-NMR: 199.2 (*s*, CO); 167.9 (*s*, $N(CO)_2$); 161.7 (*s*, =C); 134.7, 123.8 (*d*, 4 arom. CH); 131.5 (*s*, 2 arom. C); 128.1 (*d*, C(2')); 57.6 (*d*, HC(1'')); 37.4 (*t*, H_2C(4')); 29.4 (*t*, H_2C(6')); 27.9 (*t*, H_2C(5')); 24.4 (*t*, H_2C(2'')); 22.2 (*t*, H_2C(3''), H_2C(4'')); 13.7 (*q*, Me).

7.5. *3-(1,2,2-Triphenylvinyl)cyclohex-2-en-1-one* (**33a**). According to *GP A*, a soln. of **32a** (1.35 mmol) in THF (60 ml) was treated with a catalytic amount of DBU. Then, an excess of **2a** dissolved in benzene was added drop-wise. CC (hexane/AcOEt 10:1 to 1:1) yielded 200 mg (42%) of **33a**. Colorless crystals. M.p. 179–181°. IR: 3077*m*, 3053*m*, 3026*m*, 2947*m*, 2920*m*, 2878*m*, 2864*m*, 1651v*s*, 1597*s*, 1490*s*, 1454*m*, 1443*s*, 1410*m*, 1360*m*, 1344*s*, 1323*m*, 1306*m*, 1296*m*, 1253*m*, 1240*s*, 1193*m*, 1183*m*, 1154*m*, 1132*m*, 1075*m*, 884*m*, 773*s*, 762*m*, 751*m*, 726*m*, 699v*s*. ^{1}H-NMR: 7.22–6.85 (*m*, 15 arom. H); 5.76 (*t*, *J* = 1.4, CH); 2.24–2.14 (*m*, H_2C(6), H_2C(4)); 1.81–1.73 (*m*, H_2C(5)). ^{13}C-NMR: 199.4 (*s*, CO); 165.4 (*s*, C(3)); 142.9, 142.5, 142.0, 140.6 (4*s*, 3 arom. C, 2 =C)[8]); 131.2, 131.1, 130.3, 129.8, 128.1, 127.7, 127.6, 127.0, 126.9 (9*d*, 15 arom. CH, =CH); 37.3 (*t*, C(6)); 30.5 (*t*, C(4)); 23.1 (*t*, C(5)). ESI-MS: 350 (100, $M^{+\cdot}$), 273 (58, $[M - Ph]^+$), 215 (18), 165 (17).

Crystals suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2/hexane by slow evaporation of the solvent.

7.6. *3-(1,1-Diphenylhex-1-en-2-yl)cyclohex-2-en-1-one* (**33b**). According to *GP A*, a soln. of **32b** (6 mmol) in THF (60 ml) was treated with DBU (6 mmol). Then, an excess of **2a** dissolved in benzene was added drop-wise. CC (hexane/Et_2O 2:1 to 1:3) gave 480 mg (25%) of **33b**. Colorless crystals. M.p. 115–116°. IR: 2949*s*, 2923*m*, 2891*m*, 2865*m*, 2858*m*, 2844*m*, 1671*vs*, 1606*s*, 1582*m*, 1492*m*, 1446*m*, 1413*w*, 1375*w*, 1343*m*, 1322*m*, 1293*m*, 1254*s*, 1235*m*, 1186*m*, 1163*w*, 1127*m*, 1101*m*, 1077*m*, 1029*m*, 884*m*, 774*m*, 768*s*.

[8]) The signals of two of the three arom. C-atoms overlap.

^{1}H-NMR: 7.37–7.07 (*m*, 10 arom. H); 6.00 (*s*, =CH); 2.31–2.25 (*m*, $H_2C(6)$, $CH_2(Bu)$); 2.17–2.13 (*m*, $H_2C(4)$); 1.82–1.74 (*m*, $H_2C(5)$); 1.46–1.36, 1.32–1.20 (2*m*, 2 $CH_2(Bu)$); 0.84 (*t*, *J* = 7.3, Me). ^{13}C-NMR: 199.4 (*s*, CO); 166.0 (*s*, C(3)); 142.4, 142.0, 140.4, 140.1 (4*s*, 2 arom. C, 2 =C); 129.4, 129.2, 129.1, 128.0, 127.8, 127.1, 127.0 (7*d*, 10 arom. CH, =CH); 37.3 (*t*, C(6)); 34.4 (*t*, C(4)); 30.9, 30.7 (2*t*, C(5), $CH_2(Bu)$); 23.0, 22.7 (2*t*, 2 $CH_2(Bu)$); 13.7 (*q*, Me). CI-MS: 331 (100, $[M + 1]^+$). Anal. calc. for $C_{24}H_{26}O$ (330.470): C 87.23, H 7.93; found: C 87.05, H 7.97.

Crystals suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2/hexane by slow evaporation of the solvent.

8. *Reaction of (*E*)-1-Phenyl-3-piperidinoprop-2-ene-1-thione* (**34**).

8.1. *1-(2,5-Dihydro-4,5,5-triphenylthiophen-2-yl)piperidine* (**40a**). According to *GP B*, **34** (1.86 mmol) in CH_2Cl_2 (40 ml) and **2a** (*ca*. 2.5 mmol) in benzene (*ca.* 40 ml) were used. To the soln., a catalytic amount (10 mg) of $Rh_2(OAc)_4$ was added and the mixture was stirred for 4 h. The crude product was purified by CC (CH_2Cl_2/Et_2O 400:1): 365 mg (*ca.* 50%) of **40a**. Yellowish crystals. M.p. 130–133°. IR: 3055*m*, 3029*m*, 2931v*s*, 2852*s*, 2804*m*, 1633*w*, 1597*m*, 1575*m*, 1493*s*, 1465*m*, 1442*s*, 1385*w*, 1365*m*, 1335*s*, 1323*m*, 1308*m*, 1266*w*, 1237*m*, 1221*m*, 1182*w*, 1155*m*, 1115*s*, 1098v*s*, 1034*m*, 981*s*, 895*m*, 861*m*, 774*s*, 763v*s*, 736v*s*, 697v*s*. ^{1}H-NMR[9]): 7.75–6.97 (*m*, 15 arom. H); 6.19 (*d*, *J* = 2.9, HC(3')); 4.65 (*d*, *J* = 2.9, HC(2')); 2.43 (br. *s*, 2 CH_2N); 1.12 (br. *s*, 2 CH_2); 0.97 (br. *s*, CH_2). ^{13}C-NMR ((D_6)DMSO): 149.2, 144.5, 141.5, 139.8 (4*s*, 3 arom. C, C(4')); 133.1, 132.6, 129.5, 129.4, 128.6, 128.5, 128.3, 128.0, 127.8, 127.5, 127.1, 127.0, 126.8, 126.3, 126.1 (15*d*, 15 arom. CH); 117.0 (*d*, C(3')); 78.8 (*d*, C(2')); 71.4 (*s*, C(5')); 50.2 (*t*, 2 CH_2N); 25.9 (*t*, 2 CH_2); 23.8 (*t*, CH_2). CI-MS (NH_3): 398 (10, $[M + 1]^+$), 361 (10), 348 (30), 313 (100, $[M + 1 -$ piperidine$]^+$), 299 (6), 86 (9).

8.2. cis-*1-(2,5-Dihydro-4,5-diphenylthiophen-2-yl)piperidine* (*cis*-**40b**) *and* trans-*1-(2,5-Dihydro-4,5-diphenylthiophen-2-yl)piperidine* (*trans*-**40b**)**.** According to *GP B*, **34** (1.2 mmol) in toluene (10 ml) and **2b** (*ca*. 4 mmol) in toluene (*ca.* 50 ml) were used. The soln. was stirred at 80° for 4 d. After total conversion of the starting material (TLC), the soln. was cooled to r.t., the solvent was removed *i.v.*, and the crude product was purified by CC (hexane/AcOEt 10:1 + 3% NEt_3): 181 mg (49%) of a mixture of *cis*-**40b** and *trans*-**40b**,

[9]) Spectra's are not clean because of fast decomposition of the substance.

which was separated by MPLC (hexane/AcOEt 20:1 + 2% Et_3N) to give 60 mg (16%) of *cis*-**40b** and 50 mg (14%) of *trans*-**40b.**

Data of *cis*-**40b**: Oily, yellowish crystals. Mp. 106–123°. IR (Golden Gate ATR): 2934*w*, 2849*w*, 2810*w*, 1644*w*, 1601*w*, 1574*w*, 1495*w*, 1454*w*, 1439*w*, 1392*w*, 1368*w*, 1338*w*, 1309*w*, 1245*w*, 1222*w*, 1149*w*, 1100*m*, 1076*w*, 1036*w*, 977*w*, 911*w*, 860*w*, 846*w*, 773*w*, 759*m*, 724*m*, 698*s*, 688*m*. ^{1}H-NMR: 7.38–7.09 (*m*, 10 arom. H); 6.37 (*dd*, *J* = 2.4, 2.0, HC(3')); 5.92 (*dd*, *J* = 2.4, 2.0, HC(5')); 5.73 (*t*-like, *J* = 2.0, HC(2')); 2.56 (*t*-like, 2 CH_2N); 1.71–1.51 (*m*, 2 CH_2); 1.50–1.38 (*m*, CH_2). ^{13}C-NMR: 144.6, 143.0, 134.9 (3*s*, C(4'), 2 arom. C); 129.6, 128.7, 128.5, 128.3, 127.7, 127.0, 126.7 (7*d*, 10 arom. CH, C(3')); 83.3 (*d*, C(2')); 55.7 (*d*, C(5')); 50.2 (*t*, 2 CH_2N); 26.2 (*t*, 2 CH_2); 23.9 (*t*, CH_2). CI-MS (NH_3): 291 (24), 290 (100, $[M - S + 1]^+$). Anal. calc. for $C_{21}H_{25}NS$ (321.16): C 78.46, H 7.21, N 4.36, S 9.97; found: C 78.13, H 6.82, N 4.29 S 9.54.

Crystals suitable for the X-ray crystal-structure determination were grown from Et_2O/hexane by slow evaporation of the solvent.

Data of *trans*-**40b**: Pale yellowish oily crystals. M.p. 110–138°. IR (Golden Gate ATR): 2933*w*, 2877*w*, 2851*w*, 2798*w*, 1575*w*, 1496*w*, 1446*m*, 1363*w*, 1331*w*, 1208*w*, 1149*w*, 1092*m*, 1034*w*, 977*m*, 850*w*, 820*w*, 768*m*, 754*m*, 726*m*, 714*m*, 693*m*. ^{1}H-NMR: 7.33–7.07 (*m*, 10 arom. H); 6.31 (*dd*, *J* ≈ 2.5, 1.9, HC(3')); 5.99 (*dd*, *J* = 5.1, 2.5, HC(5')); 5.68 (*dd*, *J* = 5.1, 1.9, HC(2')); 2.63–2.47 (*m*, 2 CH_2N); 1.71–1.52 (*m*, CH_2); 1.49–1.42 (*m*, CH_2)). ^{13}C-NMR: 145.9 (*s*, C(4')); 142.6, 134.7 (2*s*, 2 arom. C); 129.5, 128.5, 128.2, 127.7, 127.6, 126.9 (6*d*, 10 arom. CH, C(3)); 83.3 (*d*, C(2')); 57.3 (*d*, C(5')); 49.7 (*t*, 2 CH_2N); 25.6 (*t*, 2 CH_2); 24.2 (*t*, CH_2). CI-MS (NH_3): 291 (24), 290 (100, $[M - S + 1]^+$).

8.3. *1-(2,5-Dihydro-4-phenylthiophen-2-yl)piperidine* (**40c**). According to *GP B*, **34** (1.3 mmol) in CH_2Cl_2 (20 ml) and **2c** (*ca*. 6 mmol) in THF (30 ml) were used. The crude product was purified by CC (hexane/AcOEt 2:1): 174 mg (55%) of **40c**. Yellowish oily crystals. M.p. not measurable. IR: 2932*vs*, 2852*s*, 2816*s*, 2788*s*, 2748*m*, 1639*w*, 1598*w*, 1575*w*, 1496*s*, 1468*m*, 1450*s*, 1441*s*, 1429*m*, 1384*m*, 1365*s*, 1335*s*, 1321*s*, 1304*s*, 1282*w*, 1263*w*, 1247*m*, 1232*s*, 1213*s*, 1152*s*, 1128*m*, 1116*s*, 1099*vs*, 1075*m*, 1036*m*, 994*s*, 975*s*, 964*m*, 921*m*, 863*s*, 847*s*, 776*s*, 758*vs*, 748*vs*, 713*vs*, 687*vs*, 636*m*. ^{1}H-NMR ($CDCl_3$): 7.39–7.18 (*m*, 5 arom. H); 6.14 (*q*-like, =CH); 5.72 (*q*-like, HC(2')); 3.93 (*q*-like, $H_2C(5')$); 2.50–2.36 (*m*, 2 CH_2N); 1.57–1.36 (*m*, 3 CH_2). ^{13}C-NMR: 142.2 (*s*, C(4')); 134.3 (*s*, 1 arom. C); 127.6, 127.2, 125.1 (3*d*, 5 arom. CH); 125.0 (*d*, C(3')); 83.4 (*d*, C(2')); 48.6 (*t*,

C(5')); 36.8 (*t*, 2 CH_2N); 24.7, 23.3 (2*t*, 3 CH_2). CI-MS (NH_3): 246 (100, $[M + 1]^+$), 214 (86, $[M + 1 - S]^+$), 86 (27, [piperidine +1]$^+$).

Crystals suitable for the X-ray crystal-structure determination were grown from Et_2O/hexane by slow evaporation of the solvent.

8.4. *1-(4-Phenyl-1-thiaspiro[4.5]dec-3-en-2-yl)piperidine* (**40d**). According to *GP B*, **34** (1.3 mmol) in CH_2Cl_2 (10 ml) and **2d** (*ca*. 4 mmol) in CH_2Cl_2 (*ca.* 50 ml) were used. To the soln. a catalytic amount (5 mg) of $Rh_2(OAc)_4$ was added, and the mixture was stirred at r.t. for 7 h. Then, the solvent was removed *i.v.* and the crude product was purified by CC (hexane/AcOEt 2:1): 364 mg (92%) of **40d**. Yellowish crystals. M.p. 130–133°. IR: 2933v*s*, 2853v*s*, 2752*w*, 1662*w*, 1574*w*, 1494*m*, 1441v*s*, 1363*m*, 1333*s*, 1322*m*, 1302*m*, 1262*m*, 1249*m*, 1222*m*, 1205*m*, 1157*m*, 1116*s*, 1097v*s*, 1072*m*, 1033*m*, 984v*s*, 967*w*, 904*m*, 867*m*, 766v*s*, 719*m*, 698v*s*. ^{1}H-NMR: 7.33–7.22 (*m*, 3 arom. H); 7.13–7.07 (*m*, 2 arom. H); 5.56 (*d*, *J* = 2.4, =CH); 5.45 (*d*, *J* = 2.4, HC(3')); 2.52–2.39 (*m*, 2 CH_2N); 1.79–1.38 (*m*, 8 CH_2). ^{13}C-NMR: 153.0 (*s*, 1 arom. C); 137.0 (*s*, C(4')) 129.1, 128.0, 127.6, 127.2 (4*d*, 5 arom. CH, C(3')); 79.9 (*d*, C(2')); 66.4 (*s*, C(5')); 49.9 (br. *t*, 2 CH_2N); 39.3, 37.6 (2*t*, 2 CH_2); 25.7, 25.0, 24.8, 24.2, 23.9 (5*t*, 6 CH_2). EI-MS: 313 (35, $M^{+\cdot}$), 280 (10, $[M - S - 1]^+$), 229 (95, $[M - C_5H_{10}N]^+$), 199 (40), 99 (100), 98 (91), 81 (54), 69 (24), 55 (46), 43 (66).

9. *X-Ray Crystal-Structure Determination of* **19**, **33a**, **33b**, *cis*-**40b** and **40c** (*Table* and *Figs. 1-3*)[10]). All measurements were performed on a *Nonius KappaCCD* diffractometer [25] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. The data collection and refinement parameters are given in the *Table*, and views of the molecules are shown in *Figs. 1-3*. Data reduction was performed with *HKL Denzo* and *Scalepack* [26]. The intensities were corrected for *Lorentz* and polarization effects, and with the exceptions of **33a** and **33b**, an absorption correction based on the multi-scan method [27] was applied. Equivalent reflections were merged. The structures were solved by direct methods using SIR92 [28] which revealed the positions of all non-H-atoms. In the case of **19**, the asymmetric unit contains one molecule of the heterocyclic compound plus two disordered sites for a H_2O molecule, each of which is one

[10]) CCDC- -contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Center via* http://www.ccdc.cam.ac.uk/data_request/cif.

quarter occupied, thus giving one half of a H_2O molecule in the asymmetric unit. For all structures the non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for the Me group in **33b**). The refinement of all structures was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary absorption was applied, except in the case of **19**. In **33a**, **33b**, *cis*-**40b,** and **40c**, 1, 3, 1, and 1 reflections, whose intensities were considered as extreme outliers, were omitted from the final refinement. Neutral atom scattering factors for non-H-atoms were taken from [29a], and the scattering factors for H-atoms were taken from [30]. Anomalous dispersion effects were included in F_c [31]; the values for f' and f'' were those of [29b]. The values of the mass attenuation coefficients are those of [29c]. All calculations were performed using the SHELXL97 [32] program.

Table. *Crystallographic Data of Compounds* **19**, **33a**, **33b**, *cis*-**40b**, *and* **40c**

	19	**33a**	**33b**
Crystallized from	CH_2Cl_2	CH_2Cl_2/hexane,	CH_2Cl_2/hexane
Empirical formula	$C_{43}H_{34}S_2 \cdot 0.5H_2O$	$C_{26}H_{22}O$	$C_{24}H_{26}O$
Formula weight [g mol^{-1}]	623.87	350.46	330.47
Crystal color, habit	colorless, prism	yellow, prism	colorless, prism
Crystal dimensions [mm]	0.12 × 0.22 × 0.30	0.17 × 0.22 × 0.27	0.25 × 0.30 × 0.30
Temperature [K]	160(1)	160(1)	160(1)
Crystal system	triclinic	monoclinic	orthorhombic
Space group	$P, \bar{1}$	$P2_1$	$Pca2_1$
Z	2	2	4
Reflections for cell determination	32416	1806	2521
2θ range for cell determination [°]	4–60	4–50	4–55
Unit cell parameters a [Å]	9.7018(2)	9.9821(5)	22.0889(5)
b [Å]	13.0899(3)	9.4828(4)	9.7500(2)
c [Å]	13.9694(2)	10.7165(5)	8.8389(2)
α [°]	85.716(1)	90	90
β [°]	83.236(1)	107.853(2)	90
γ [°]	75.462(1)	90	90
V [Å^3]	1703.41(6)	965.56(8)	1903.61(7)
D_x [g cm^{-3}]	1.216	1.205	1.153
μ(MoK_α) [mm^{-1}]	0.187	0.0714	0.0682
Scan type	ϕ and ω	ω	ϕ and ω
2θ (max) [°]	60	50	55
Transmission factors (min; max)	0.867; 0.982	-	-
Total reflections measured	46930	12782	26913
Symmetry independent reflections	9964	1803	2328
Reflections with $I > 2\sigma(I)$	7526	1634	1915
Reflections used in refinement	9959	1802	2325
Parameters refined	424	245	228
Final R (F) [I > $2\sigma(I)$ reflections]	0.0465	0.0448	0.0424
wR (F^2) (all data)	0.1271	0.1178	0.1063
Weighting parameters (a; b)[a]:	0.0582; 0.6749	0.0639; 0.2654	0.0552; 0.1724
Secondary extinction coeff.	-	0.05(1)	0.026(4)
Goodness of fit	1.018	1.054	1.057
Final Δ_{max}/σ	0.001	0.001	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.53; -0.32	0.28; -0.18	0.19; -0.15

[a]) $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$ where $P = (F_o^2 + 2F_c^2)/3$

Table. *Crystallographic Data of Compounds* **19**, **33a**, **33b**, *cis*-**40b**, *and* **40c** *(continued)*

	***cis*-40b**	**40c**
Crystallized from	Et_2O/hexane	Et_2O/hexane
Empirical formula	$C_{21}H_{23}NS$	$C_{15}H_{19}NS$
Formula weight [g mol^{-1}]	321.48	245.38
Crystal color, habit	yellow, prism	red, plate
Crystal dimensions [mm]	0.10 × 0.15 × 0.17	0.03 × 0.13 × 0.13
Temperature [K]	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	$C2/c$
Z	4	8
Reflections for cell determination	73098	18871
2θ range for cell determination [°]	4–60	4 – 50
Unit cell parameters a [Å]	12.3385(2)	24.832(1)
b [Å]	5.9839(1)	5.1847(2)
c [Å]	23.8454(5)	21.2611(9)
α [°]	90	90
β [°]	91.564(1)	109.014(3)
γ [°]	90	90
V [Å^3]	1759.91(6)	2587.9(2)
D_x [g cm^{-3}]	1.213	1.259
μ(MoK_α) [mm^{-1}]	0.183	0.227
Scan type	ϕ and ω	ϕ and ω
2θ(max) [°]	60	50
Transmission factors (min; max)	0.884; 0.985	0.891; 0.996
Total reflections measured	49425	19009
Symmetry independent reflections	5157	2279
Reflections with $I > 2\sigma(I)$	3741	1623
Reflections used in refinement	5156	2278
Parameters refined	209	155
Final R (F) [$I > 2\sigma(I)$ reflections]	0.0496	0.0561
wR (F^2) (all data)	0.1261	0.1418
Weighting parameters (a; b)[a]:	0.0555; 0.6236	0.0577; 4.4843
Secondary extinction coeff.	0.041(3)	0.013(1)
Goodness of fit	1.046	1.097
Final Δ_{max}/σ	0.001	0.001
$\Delta\rho$(max; min) [e Å^{-3}]	0.31; -0.25	0.31; -0.25

[a]) $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$ where $P = (F_o^2 + 2F_c^2)/3$

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Chapter 7

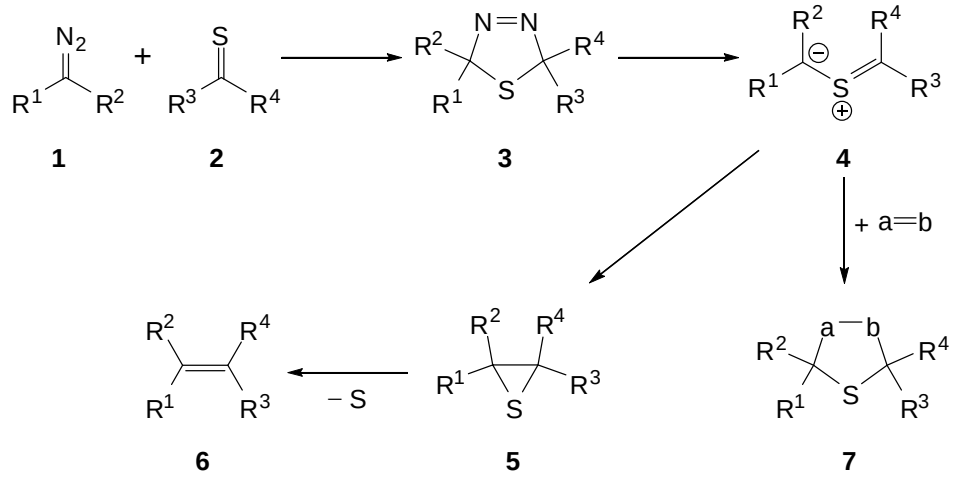
Reactions of α,β-Unsaturated Thioamides with Diazo Compounds [1])

Several reactions of the α,β-unsaturated thioamide **8** with diazo compounds **1a-1d** were investigated. The reactions with CH_2N_2 (**1a**), diazocyclohexane (**1b**), and phenyldiazomethane (**1c**) proceeded *via* a 1,3-dipolar cycloaddition of the diazo dipole at the C,C-double bond to give the corresponding 4,5-dihydro-1*H*-pyrazole-3-thiocarboxamide **12a-12c**, *i.e.*, the regioisomer which arose from the bond formation of the N-terminus of the diazo compound with the α-C-atom of **8**. In the reaction of **1a** with **8**, the initially formed cycloadduct, the 4,5-dihydro-3*H*-pyrazole **11a**, was obtained after short reaction time. In the case of **1c** two tautomers **12c** and **12c'** were formed, which, by derivatization with 2-chlorobenzoyl chloride **14**, led to the crystalline products **15** and **15'**. Their structures were established by X-ray crystallography. In the reaction of **8** and ethyl diazoacetate (**1d**), the opposite regioisomer **13** was formed. The monosubstituted thioamide **16** reacted with **1a** to give the unstable 4,5-dihydro-1*H*-pyrazole-3-thiocarboxamide **17**.

1. Introduction. – In the last twenty years, reactions of thioketones with diazo compounds have been investigated extensively. It is generally accepted that the attack of the diazo compound **1** at the thioketone **2** leads to a 2,5-dihydro-1,3,4-thiadiazole **3**, which, in general, at room temperature is not stable and undergoes a 1,3-dipolar cycloreversion by elimination of N_2 to give the intermediate thiocarbonyl ylide **4**. This reactive intermediate can undergo different reactions to yield stable products (for reviews see [1][2]). On the one hand, a 1,3-dipolar electrocyclization can take place to give the thiirane **5**, or, by subsequent desulfurization, to yield the olefin **6**. On the other hand, **4** can react with a dipolarophile in a 1,3-dipolar cycloaddition to give the corresponding heterocycles **7** (*Scheme 1*). Furthermore, stabilization of **4** *via* dimerization or [1,4]-H shift have also been reported.

[1]) D. H. Egli, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2006**, *89*, 2815.

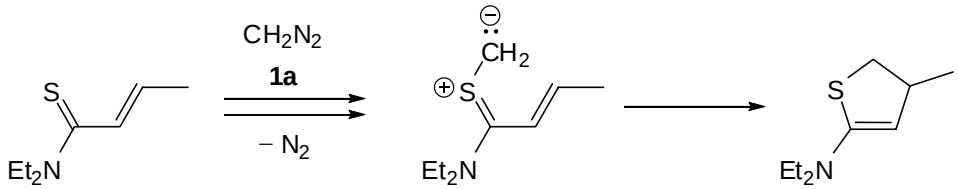
Scheme 1



Investigations concerning 1,3-dipolar cycloadditions of diphenyldiazomethane (**1**, $R^1 = R^2$ = Ph) with different dipolarophiles by *Huisgen* and *Langhals* have shown that thiones **2**, especially aromatic ones, react extremely fast with diazo compounds and, therefore, were denominated as "superdipolarophiles" [3]. Thioamides have not been included in these comparative studies, but amino substituents in 4-position of thiobenzophenone led to a decrease of the reaction rate. As diazo compounds are classified as relatively electron-rich dipoles [4] and, therefore, electron-poor dipolarophiles are suitable for an optimal HOMO-LUMO-interaction [5], it is a moot point whether thioamides, as relatively electron-rich dipolarophiles undergo a 1,3-dipolar cycloaddition with diazo compounds and the subsequent cycloreversion to give the intermediate thiocarbonyl ylides. Studies of *El-Sharif et al.* have shown that, in some cases, it is possible to generate thiocarbonyl ylide intermediates from thioamides, which led *via* 1,3-dipolar electrocyclization and subsequent desulfurization to the corresponding olefins [6].

The aim of the present work was to clarify whether unsaturated thioamides like (*E*)-*N*,*N*-diethylbut-2-enethioamide (**8**) react with diazo compounds in the manner described above, or if the dipolarophilicity of the C,C-double bond exceeds that of the C=S group. If the cycloaddition at the C=S group would be preferred, a thiocarbonyl ylide of type **9** with an extended π-system (*i.e.* R^2 = MeCH=CH) could be formed (*Scheme 2*). The latter should be able to undergo a 1,5-dipolar electrocyclization to give 2,3-dihydrothiophene **10**. Analogous 1,5-dipolar electrocyclizations of thiocarbonyl ylides bearing C=O [7-9] (and refs. cited therein), C=S [9], and C=N groups [10] have been reported recently.

Scheme 2



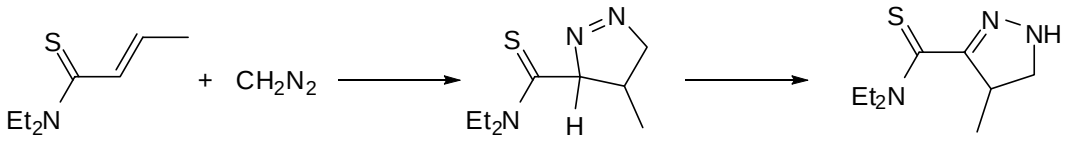
8 **9** **10**

2. Results and Discussion. – Solutions of thioamide **8** [11] in CH_2Cl_2 reacted with different diazo compounds at room temperature without any catalyst within a few hours or days to give the corresponding 1:1 adducts in good yields. According to the MS- and NMR-spectra, the resulting products have not been formed by an attack of the diazo compound at the thiocarbonyl group as it was observed in the cases of the reactions with thioketones [7-9]. In the ^{13}C-NMR spectra of the products, a signal at *ca.* 190 ppm, which is characteristic for the thioamide C-atom, was present, and the CI-MS spectra showed a $[M + 1]^+$-peak of the 1:1-adducts indicating that no N_2 elimination occurred. Thus, we proposed a 1,3-dipolar cycloaddition of the diazo component at the C,C-double bond conjugated with the C=S group. The formation of an intermediate thiocarbonyl ylide can be consequently excluded.

Investigations of the main product of the reaction of **8** with diazomethane (**1a**) obtained after a reaction time of 1 d by using two-dimensional NMR- (HMBC) and ^{15}N-NMR methods show that it consists of a 4,5-dihydro-1*H*-pyrazole and a *N*,*N*-diethylthioamide group. If the reaction was quenched after 1 h by adding AcOH and the work up was carried out quickly, two isomeric products **11a** and **12a** were obtained, whereof **11a** disappeared after a few h to give **12a** (*Scheme 3*). The less stable isomer **11a** is the result of a 1,3-dipolar cycloaddition, and a subsequent rearrangement *via* a [1,3]-H shift and leads to the more stable product **12a**.

It is surprising that no further reaction of the rearranged product with the diazo component could be observed. In a control experiment, **1a** was added to the pure product **12a**, but even stirring of the mixture at room temperature for 2 d did not result in a new product.

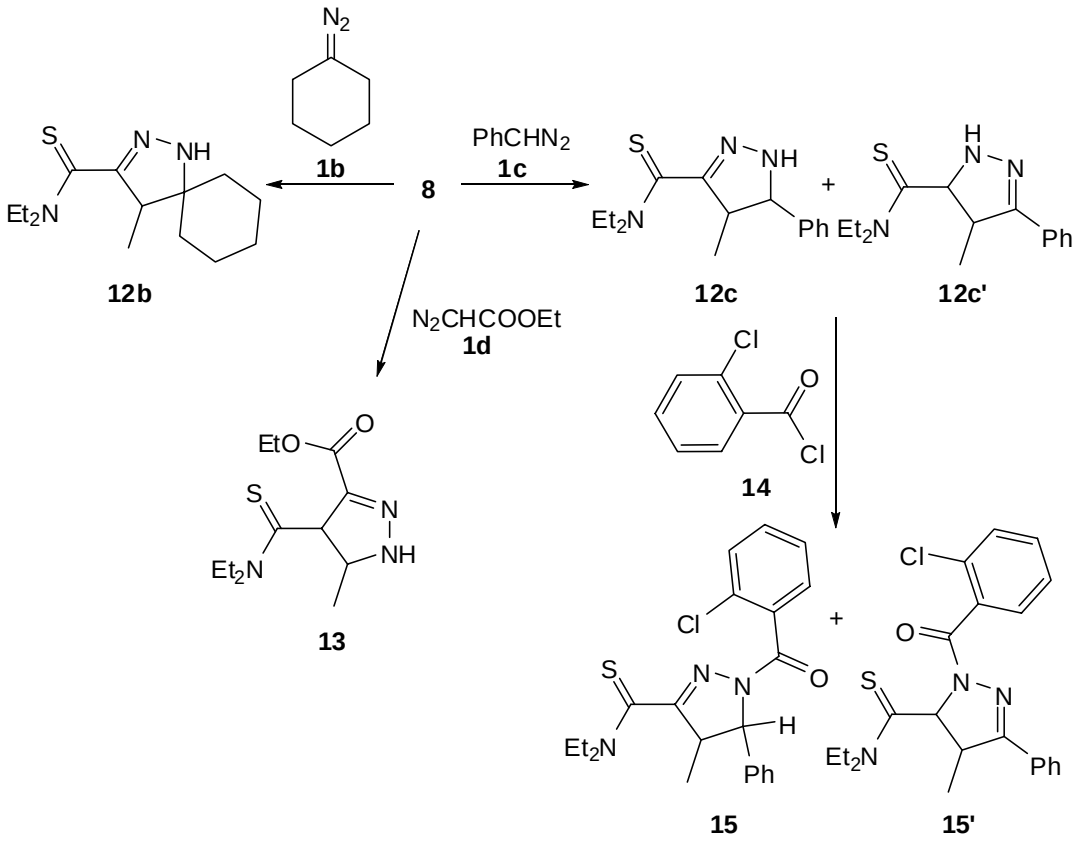
Scheme 3



8 **1a** **11a** **12a**

The reactions of **8** with diazocyclohexane (**1b**) and phenyldiazomethane (**1c**), respectively, occurred in a similar way. Although an intermediate could be detected by TLC - most likely the initial [2 + 3]-cycloadduct of type **11** – only **12b** was isolated in the first case (*Scheme 4*). Two isomeric 1:1 adducts were obtained in the reaction with **1c**, but none was the initial adduct of type **11**. Both isomers showed an NH absorption in the ^{1}H-NMR spectrum (*s* at 5.72-5.18 ppm) and a C=N signal at 155.6 ppm in the ^{13}C-NMR spectrum. The isomers could not be separated but interconverted quickly. On this basis we proposed the two tautomeric structures **12c** and **12c'**. Derivatization with 2-chlorobenzoyl chloride led to the crystalline benzoyl derivatives **15** and **15'** (*Scheme 4*), which were separated by means of chromatography. Recrystallization from hexane/CH_2Cl_2 yielded suitable crystals for the X-ray crystal-structure determination (*Fig.*).

Scheme 4



12b **12c** **12c'** **13** **14** **15** **15'**

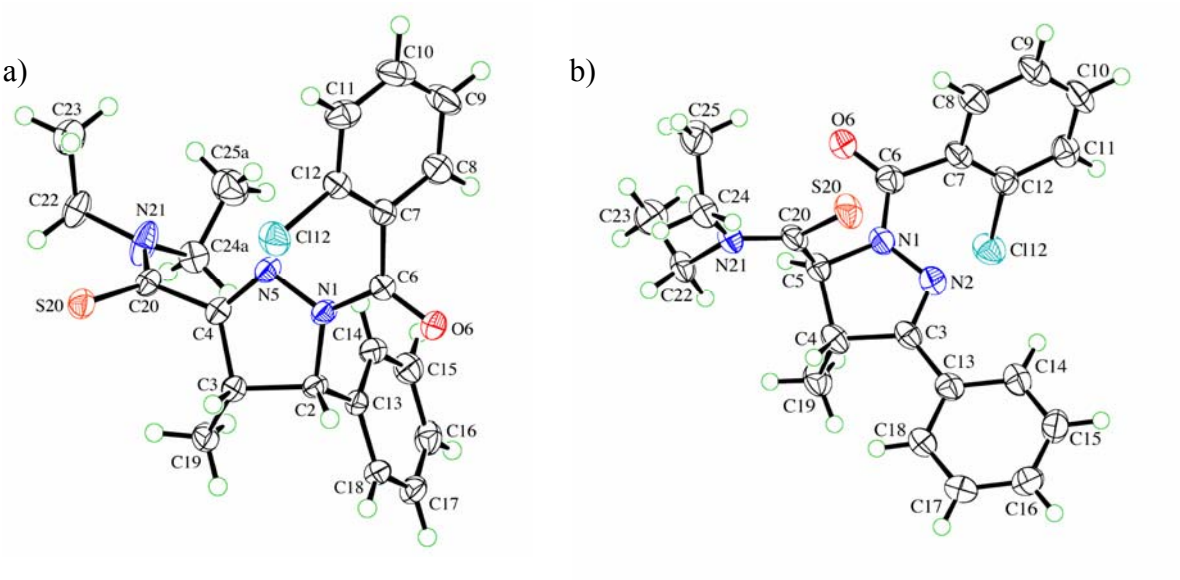


Fig. *ORTEP Plots* [12] *of the molecular structure of a) one of the two conformations of* **15***, and b)* **15'** (50% probability ellipsoids, arbitrary numbering of the atoms)

Since the space group of **15** is centrosymmetric, the compound in the crystal is racemic. The Me and Ph substituents on the five-membered ring are in a *cis* configuration. One of the Et groups of the diethylamino group is disordered over two equally occupied orientations as a result of random inversion of the position of the lone pair of electrons on the N-atom. The compound has crystallized in a space group that would allow for an enantiomerically pure compound, but refinement of the absolute structure parameter indicates that the crystals are most likely inversion twins. The five-membered ring of **15'** has a slightly flattened envelope conformation with atom C(5) as the envelope flap. The substituents at atoms C(4) and C(5) have a *trans* relationship.

The crystal-structure determination of the derivatives **15** and **15'** proved that the reaction of **8** with **1c** occurred regioselectively, but led to a mixture of two tautomers[2]), namely the 3-thiocarboxamide **12c** and the 5-thiocarboxamide **12c'** (*Scheme 4*). An explanation of the formation of **12c'** is the conjugation of the C=N bond with the Ph group at C(3).

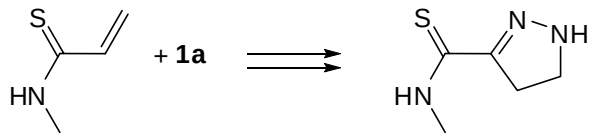
The 1,3-dipolar cycloadditions of **8** with **1a-1c** proceeded all with the same regioselectivity, *i.e.*, the N-terminus of the diazo compound reacted with the α-C-atom of the thioamide to give the intermediate 4,5-dihydro-3*H*-pyrazole-3-thiocarboxamides of

[2]) In the reaction of **8** with **1a** and **1b**, respectively, only the formation of the isomer with the C=N bond conjugated with the thioamide group, *i.e.* **12a** and **12b**, respectively, was observed.

type **11** (*Scheme 3*)[3]). On the other hand, the addition of ethyl diazoacetate (**1d**) with **8** led to the 4,5-dihydro-1*H*-pyrazole **13** (*Scheme 4*), which bears the thiocarboxamide group at C(4). Therefore, the C-terminus of the diazo dipole reacted with the α-C-atom of the thioamide.

The reaction of the N-monosubstituted α,β-unsaturated thioamide **16** with **1a** at room temperature led within a few min to an unstable product, which decomposed quickly. The NMR-spectra of the crude product indicated the formation of the corresponding thioamide **17** with a 4,5-dihydro-1*H*-pyrazole residue (*Scheme 5*).

Scheme 5



16 **17**

3. Conclusions. – In all reactions of thioamide **8** with diazo compounds **1a-1d**, an addition of the dipole onto the C,C-double bond of **8** took place exclusively. Surprisingly, no addition onto the C=S group could be observed. The formed products are the corresponding dihydropyrazole thioamides **12a-12c** and **13**. In the cases of **12a-12c**, the products were formed in a regioselective cycloaddition, in which the N-terminus of the diazo compound added to the α-C-atom of **8**, followed by a [1,3]-H shift. The α,β-unsaturated thioamide **16** reacted with **1a** analogously, but the corresponding product **17** is extremely unstable. In the case of the reaction of **8** with **1d**, the C-terminus of the diazo compound added to the α-C-atom of **8** to give the opposite regioisomer **13**. In summary, in reactions with diazo compounds, the C=S group of α,β-unsaturated thioamides is less reactive than the C=C bond and therefore, thioamides of type **8** and **16** are no suitable precursors for the generation of thiocarbonyl ylides.

We thank the analytical units of our institute for spectra and analyses, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for financial support.

[3]) This regioselectivity is supported by the examination of the orbital coefficients of the HOMO (**1a**, **1c**) and the LUMO (**8**) calculated with AMPAC version 8.16.7 with the AM1-Hamilton. Unfortunately, the results of the analogous calculations for the reaction with ethyl diazoacetate (**1d**) are not in accordance with the different regioselectivity of the cycloaddition. We thank *Dr. R. W. Kunz* for carrying out the calculations.

Experimental Part

1. *General.* See [9]. For the assignment of ^{15}N signals, ^{15}N-HMBC 2D-NMR methods were employed.

2. *Starting Materials.* The thioamides and diazo compounds were prepared following known protocols: diazomethane (**1a**) [13], diazocyclohexane (**1b**) [14], phenyldiazomethane (**1c**) [15], (*E*)-*N*,*N*-diethylbut-2-enethioamide (**8**) [11], *N*-ethylprop-2-enethioamide (**16**) [16]. All other reagents are commercially available.

3. *Reaction of (*E*)-*N,N*-Diethylbut-2-enethioamide* (**8**) *with Diazo Compounds.*

3.1. N,N-*Diethyl-4,5-dihydro-4-methyl-3*H-*pyrazole-3-thiocarboxamide* (**11a**) *and* N,N-*Diethyl-4,5-dihydro-4-methyl-1*H-*pyrazole-3-thiocarboxamide* (**12a**). To a soln. of **8** (1.0 mmol) in CH_2Cl_2 (10 ml) was added drop-wise a soln. of **1a** (*ca.* 2 mmol) in Et_2O (6 ml). After 2 h, AcOH (*ca.* 10 drops) was added to quench the reaction. Purification of the crude product by CC (hexane/AcOEt 1:4 to 1:1) afforded 92 mg (45%) of **11a** and 66 mg (33%) of **12a**. Data of **11a**: R_f-value: (hexane/AcOEt 1:1): 0.15. Yellowish oil. IR (neat): 3306*m*, 2971v*s*, 2934v*s*, 2873*s*, 1688*m*, 1549*m*, 1505v*s*, 1454v*s*, 1428v*s*, 1381v*s*, 1359v*s*, 1305v*s*, 1272v*s*, 1233v*s*, 1139*s*, 1095*s*, 1077*s*, 980*w*, 921*m*, 888*w*, 856*w*, 836*m*, 783*w*, 757*w*, 736*m*. ^{1}H-NMR: 5.26–5.23 (*m*, HC(3)); 4.95–4.85 (*dq*-like, 1 H of $H_2C(5)$); 4.39–4.14 (*m*, 1H of $H_2C(5)$, MeCH_2N); 3.96–3.76 (*m*, MeCH_2N); 3.00–2.91 (*m*, HC(4)); 1.44 (*t*, *J* = 7.2, *Me*CH_2N); 1.31 (*t*, *J* = 7.1, *Me*CH_2N); 1.03 (*d*, *J* = 7.1, *Me*CH(4)). ^{13}C-NMR: 194.3 (*s*, CS); 99.1 (*d*, C(3)); 85.4 (*t*, C(5)); 48.5, 46.5 (2*t*, 2 CH_2N); 33.2 (*d*, C(4)); 18.5 (*q*, *Me*C(4)); 14.1, 10.9 (2*q*, 2 *Me*CH_2N). CI-MS (NH_3): 200 (100, $[M + 1]^+$), 172 (33, $[M + 1 - N_2]^+$).

Data of **12a**: R_f-value: (hexane/AcOEt 1:1): 0.1. Yellowish oil. IR (neat): 3295*m*, 2971*m*, 2934*m*, 2872*w*, 1502v*s*, 1431*s*, 1379*m*, 1360*w*, 1344*w*, 1304*m*, 1271*s*, 1251*m*, 1227*w*, 1208*m*, 1140*m*, 1114*w* 1076*w*, 1003*w*, 969*w*, 921*w*, 819*w*, 779*w*, 760*w*. ^{1}H-NMR: 5.50–5.00 (br. *s*, NH); 4.41–4.27 (*m*, MeCH_2N); 4.15–3.97 (*m*, MeCH_2N, HC(4), 1 H of $H_2C(5)$), 3.39 (*t*, *J* = 8.1, 1 H of $H_2C(5)$); 1.65–1.53 (*m*, 2 *Me*CH_2N); 1.50 (*d*, *J* = 6.8, *Me*HC(4)). ^{13}C-NMR: 189.6 (*s*, CS); 156.7 (*s*, C(3)); 55.1 (*t*, C(5)); 47.8, 46.4 (2*t*, 2 CH_2N); 43.1 (*d*, C(4)); 15.5, 14.2 (2*q*, 2 *Me*CH_2N); 11.0 (*q*, *Me*HC(4)). CI-MS (NH_3): 200 (100, $[M + 1]^+$).

In an analogous experiment, to a soln. of **8** (1.3 mmol) in dry THF (10 ml) was added drop-wise a soln. of **1a** (*ca.* 3 mmol) in THF (*ca*. 8 ml). Then, the mixture was stirred for 1

d at r.t. Purification of the crude product by CC (hexane/AcOEt 1:2) afforded 218 mg (84%) of (**12a**) as a single product.

3.2. N,N-*Diethyl-4-methyl-1,2-diazaspiro[4.5]deca-2-en-3-thiocarboxamide* (**12b**). To a soln. of **8** (200 mg, 1.3 mmol) in CH_2Cl_2 (10 ml) was added drop-wise a soln. of **1b** (*ca.* 2 mmol) in CH_2Cl_2 (40 ml) and the mixture was stirred at r.t. for 6 h. Purification of the crude product by CC (hexane/AcOEt 1:2) afforded 283 mg (81%) of **12b**. Yellowish crystals. M.p. 74–76°. IR (KBr): 3329*s*, 2966*m*, 2928*vs*, 2856*m*, 1622*w*, 1579*m*, 1512*vs*, 1451*s*, 1437*s*, 1405*m*, 1372*m*, 1356*m*, 1319*w*, 1297*m*, 1285*m*, 1267*s*, 1248*s*, 1209*m*, 1135*m*, 1097*m*, 1075*m*, 1061*m*, 1039*w*, 1019*m*, 981*w*, 948*m*, 936*w*, 916*m*, 855*w*, 844*w*, 831*w*, 809*w*, 781*m*, 738*s*, 698*s*, 666*vs*. ^{1}H-NMR: 5.2–4.7 (br. *s*, NH); 4.00–3.90, 3.73–3.65 (2*m*, 2 CH_2N); 3.31 (*q*, *J* = 7.3, HC(4)); 1.58–1.37 (*m*, 5 CH_2); 1.36–1.13 (*m*, 2 *Me*CH_2N); 0.96 (*d*, *J* = 7.3, MeC(4)). ^{13}C-NMR: 190.0 (*s*, CS); 156.4 (*s*, C(3)); 67.0 (*s*, C(5)); 50.3 (*d*, C(4)); 47.8, 46.5 (2*t*, 2 CH_2N); 36.3, 30.3, 25.4, 23.5, 22.6 (5*t*, cyclohexyl CH_2); 14.3, 11.0 (2*q*, 2 *Me*CH_2N); 10.1 (*q*, *Me*C(4)). EI-MS: 267 (86, $M^{+\cdot}$), 252 (41, $[M - Me]^+$), 224 (56, $[M - Me - N_2]^+$), 151 (36, $[M - SNEt_2]^+$), 98 (59, $C_6H_{12}N^+$), 72 (100, Et_2N^+).

3.3. N,N-*Diethyl-4,5-dihydro-4-methyl-5-phenyl-1*H-*pyrazole-3-thiocarbox-amide* (**12c**) *and* N,N-*Diethyl-4,5-dihydro-4-methyl-3-phenyl-1*H-*pyrazole-5-thiocarboxamide* (**12c'**)[4]). To a soln. of **8** (843 mg, 5.2 mmol) in toluene (30 ml) was added drop-wise a soln. of **1c** (*ca.* 7 mmol) in toluene (150 ml) over a period of 3 d. Purification of the crude product by CC (hexane/AcOEt 8:1 to 2:1) afforded 563 mg (52%) of a mixture of the two isomeric thioamides **12c** and **12c'** as an oil and 197 mg of the starting material. Data of **12c**: ^{1}H-NMR: 7.74–7.69 (*d*-like, 1 arom. H); 7.43–7.31 (*m*, 4 arom. H); 5.72–5.18 (*br. s*, NH); 4.41 (*d*, *J* = 2.8, HC(5)); 4.25–3.62 (*m*, 2 CH_2N); 3.54 (*dq*; *J* = 2.8, 7.2, HC(4)); 1.52 (*d*, *J* = 7.2, MeC(4)); 1.44-1.32 (*m*, 2 *Me*CH_2N). ^{13}C-NMR: 201.5 (*s*, CS); 155.6 (*s*, C(5)); 131.5 (*s*, 1 arom. C); 128.4, 127.5, 126.4 (3*d*, 5 arom. CH); 71.6 (*d*, C(3)); 48.7 (*t*, CH_2N); 48.0 (*d*, C(4)); 45.5 (*t*, CH_2N); 17.9 (q, *Me*C(4)); 14.3, 13.3 (2*q*, 2 *Me*CH_2N). CI-MS (NH_3, mixture): 276 (100, $[M + 1]^+$), 264 (36).

Data of **12c'**: ^{1}H-NMR: 7.74-7.69 (*d*-like, 1 arom. H); 7.43–7.31 (*m*, 4 arom. H); 5.72–5.18 (*br. s*, NH); 5.11 (*d*, *J* = 10.1, HC(3)); 4.25–3.79 (*m*, 2 CH_2N, HC(4)); 1.44–1.32 (*m*, 2

[4]) The tautomers **12c** and **12c'** could not be separated by HPLC because of a fast tautomerization. As it was not possible to isolate one of the two isomers in pure form, the correlation of the NMR signals with the arom. C-atoms and Et groups are not absolutely clear.

MeCH_2N); 0.77 (*d*, *J* = 8.4, MeC(4)). ^{13}C-NMR: 189.2 (*s*, CS); 155.6 (*s*, C(3)); 137.7 (*s*, 1 arom. C); 128.8, 128.3, 127.2 (3*d*, 5 arom. CH); 68.3 (*d*, C(5)); 47.9 (*t*, CH_2N); 46.8 (*d*, C(4)); 46.7 (*t*, CH_2N); 11.3 (*q*, *Me*C(4)); 11.0, 10.9 (2*q*, 2 *Me*CH_2N).

3.4. N,N-*Diethyl-1-(2-chlorobenzoyl)-4,5-dihydro-4-methyl-5-phenyl-1*H-*pyrazole-3-thiocarboxamide* (**15**) *and* N,N-*Diethyl-1-(2-chlorobenzoyl)-4,5-dihydro-4-methyl-3-phenyl-1*H-*pyrazole-5-thiocarboxamide* (**15'**). To a soln. of a mixture of **12c** and **12c'** (275 mg, 1 mmol) in CH_2Cl_2 (20 ml) was added 2-chlorobenzoyl chloride (**14**, 174 mg, 1 mmol) and Et_3N (111 mg). After 15 min, the mixture was poured on ice (50 g) and diluted with CH_2Cl_2 (30 ml). After separation of the two phases, the aq. phase was extracted with CH_2Cl_2, the org. phase was dried ($MgSO_4$), and the solvent was evaporated. Purification of the crude product by CC (hexane/AcOEt 5:1) afforded 163 mg of **15** (40%), 100 mg of **15'** (25%), and 84 mg (20%) of a mixture of the two isomers. Data of **15**: Yellowish crystals. M.p. 161–162°. IR (Golden Gate ATR): 3056*w*, 3031*w*, 2973*w*, 2935*w*, 2874*w*, 1634*m*, 1594*w*, 1579*w*, 1508*m*, 1493*w*, 1473*m*, 1444*m*, 1422*m*, 1380*w*, 1363*w*, 1309*w*, 1297*w*, 1282*w*, 1264*m*, 1253*m*, 1221*m*, 1201*w*, 1173*w*, 1139*m*, 1092*w*, 1076*w*, 1055*m*, 1037*w*, 979*w*, 918*w*, 841*m*, 822*m*, 772*m*, 746*s*, 691*s*. ^{1}H-NMR: 7.40–7.25 (*m*, 9 arom. H); 5.74 (*d*, *J* = 11.6, HC(5)); 4.41 (*dq*, *J* = 11.6, 7.6, HC(4)); 4.21–4.10 (*m*, 1 H of CH_2N); 3.83–3.64 (*m*, 2 H of 2 CH_2N); 3.58–3.47 (*m*, 1 H of CH_2N); 1.24, 1.11 (2*t*, *J* = 7.1, 2 *Me*CH_2N); 0.76 (*d*, *J* = 7.6, MeC(4)). ^{13}C-NMR: 187.1 (*s*, CS); 165.7 (*s*, CO); 158.4 (*s*, C(3)); 135.8, 130.8 (2*s*, 2 arom. C)[5]); 130.2, 129.1, 128.8, 128.5, 127.8, 126.8, 126.5 (7*d*, 9 arom. CH); 64.0 (*d*, C(5)); 48.3 (*t*, CH_2N); 47.7 (*d*, C(4)); 46.4 (*t*, CH_2N); 14.1 (*q*, *Me*C(4)); 11.9, 10.8 (2*q*, 2 *Me*CH_2N). CI-MS (NH_3): 416 (41), 415 (25), 414 (100, $M^{+\cdot}$). Anal. calc. for $C_{22}H_{24}ClON_3S$ (413.96): C 63.83, H 5.84, Cl 8.56, N 10.15, S 7.75; found: C 63.80, H 5.77, Cl 8.56, N 10.07, S 7.84.

Crystals suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2/hexane by slow evaporation of the solvent.

Data of **15'**: Colorless crystals. M.p. 176–179°. IR (Golden Gate ATR): 3066*w*, 2975*w*, 2939*w*, 2873*w*, 2833*w*, 1982*w*, 1962*w*, 1839*w*, 1637*m*, 1592*w*, 1567*w*, 1503*m*, 1454*m*, 1440*m*, 1421*m*, 1378*w*, 1306*w*, 1224*w*, 1155*w*, 1089*w*, 1059*w*, 833*w*, 784*m*, 770*m*, 745*m*, 692*m*. ^{1}H-NMR: 7.62–7.57 (*m*, 3 arom. H); 7.43–7.26 (*m*, 6 arom. H); 5.35 (*d*, *J* = 3.3, HC(3)); 4.26–4.07 (*m*, 2 H of 2 CH_2N); 4.26–3.67 (*m*, 2 H of CH_2N, HC(4)); 1.49–1.44 (*m*,

[5]) The signal of the arom. CCl could not be detected. Perhaps the signal overlaps with the signal at 135.8 ppm, which is more intensive than expected.

MeCH_2N, MeC(4)); 1.32 (*t*, *J* = 7.1, *Me*CH_2N). ^{13}C-NMR: 198.4 (*s*, CS); 165.3 (*s*, CO); 159.4 (*s*, C(5)); 135.2, 131.3 (2*s*, 2 arom. C)[6]); 130.3, 130.0, 129.7, 129.1, 128.5, 127.2, 126.3 (7*d*, 9 arom. CH); 68.5 (*d*, C(3)); 49.0 (*t*, CH_2N); 48.9 (*d*, C(4)); 46.5 (*t*, CH_2N); 18.5, 14.5, 10.9 (3*q*, 2 *Me*CH_2N, *Me*C(4)). CI-MS (NH_3): 416 (45), 415 (27), 414 (100, $M^{+\cdot}$).

Crystals suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2/hexane by slow evaporation of the solvent.

3.5. *4-Ethyl (*N,N-*Diethylthiocarbamoyl)-4,5-dihydro-5-methyl-1*H-*pyrazole-3-carboxylate* (**13**). To a soln. of **8** (200 mg, 1.3 mmol) in CH_2Cl_2 (10 ml) was added drop-wise a soln. of **1d** (*ca.* 6 mmol) in CH_2Cl_2 (20 ml) over a period of 3 d whereas the mixture was maintained at 45°. Purification of the crude product by CC (hexane/AcOEt 1:2) afforded 184 mg (50%) of **13**. IR (KBr): 3315*m*, 2978*s*, 2935*s*, 2874*m*, 1703v*s*, 1578*s*, 1503v*s*, 1450v*s*, 1426v*s*, 1374*s*, 1344*s*, 1304*s*, 1272v*s*, 1223v*s*, 1172*m*, 1132v*s*, 1079v*s*, 1019v*s*, 942*w*, 921*w*, 831*m*, 770*m*, 739*m*. ^{1}H-NMR: 7.45–6.80 (br. *s*, NH); 4.32 (*d*, *J* = 3.3, HC(4)); 4.28 (*q*, *J* = 7.1, CH_2O); 4.19 (*m*; 1 H of CH_2N); 3.80–3.66 (*m*, 2 H of 2 CH_2N); 3.62–3.50 (*m*, 1 H of CH_2N); 3.25 (*dq*, *J* = 7.2, 3.3, HC(5)); (*d*, *J* = 7.2, MeC(5)); 1.38–1.32 (2*t*, *J* = 7.1, 7.2, *Me*CH_2O, *Me*CH_2N); 1.28–1.25 (*t*, *J* = 7.1, *Me*CH_2N). ^{13}C-NMR: 200.0 (*s*, CS); 161.8 (*s*, COOEt); 146.3 (*s*, C(3)); 72.3 (*d*, C(4)); 61.1 (*t*, CH_2O); 48.7 (*t*, CH_2N); 46.9 (*d*, C(5)); 45.3 (*t*, CH_2N); 17.4 (*q*, *Me*C(5)); 14.1 (*q*, *Me*CH_2O); 13.2, 10.8 (2*q*, 2 *Me*CH_2N). CI-MS (NH_3): 289 (9, $[M + NH_4]^+$), 272 (100, $[M + 1]^+$), 244 (34, $[M - N_2 + 1]^+$).

4. *Reaction of* N-*Methylprop-2-enethioamide* (**16**) *with* **1a**. To a soln. of **16** (2.0 mmol) in THF (10 ml) was added drop-wise a soln. of **1a** (*ca.* 3 mmol) in THF (8 ml) at r.t., and the mixture was stirred for 10 min. The crude product was purified by flash-CC (hexane/AcOEt 3:1 to 1:2): *ca.* 100 mg (*ca.* 50%) of *N*-methyl-4,5-dihydro-1*H*-pyrazole-3-thiocarboxamide (**17**). Yellowish oil[7]). ^{1}H-NMR: 8.60–8.10 (br. *s*, MeN*H*); 6.10–5.50 (br. *s*, HN(1)); 3.55–3.48 (*t*-like, H_2C(5)); 3.16 (*d*, MeN); 3.14–3.03 (*t*-like, H_2C(4)). ^{13}C-NMR: 188.3 (*s*, CS); 151.4 (*s*, C(3)); 49.3 (*t*, H_2C(5)); 32.5 (*t*, H_2C(4)); 31.9 (*q*, MeN).

[6]) The signal of the arom. CCl could not be detected.

[7]) The product **17** is extremely unstable.

5. *X-Ray Crystal-Structure Determination of* **15** and **15'** (*Table* and *Figure*)[8]). All measurements were performed on a *Nonius KappaCCD* diffractometer [17] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. The data collection and refinement parameters are given in the *Table*, and views of the molecules are shown in the *Figure*. Data reduction was performed with *HKL Denzo* and *Scalepack* [18]. The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multi-scan method [19] was applied. Equivalent reflections, other than *Friedel* pairs (in **15'**), were merged. The structures were solved by direct methods using SIR92 [20], which revealed the positions of all non-H-atoms. In the case of **15**, one of the Et groups of the Et_2N group is disordered over two orientations. Two sets of positions were defined for the atoms of this Et group and the site occupation factors of the major conformation refined to a value close to 0.5, so the site occupation factors were fixed at 0.5 thereafter. Similarity restraints were applied to the chemically equivalent bond lengths and angles involving the ordered and disordered Et groups, while neighboring atoms within and between each conformation of the disordered Et group were restrained to have similar atomic displacement parameters. The non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined by using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent atom ($1.5U_{eq}$ for the Me groups). The refinement of the structures was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied. In the case of **15**, 6 reflections, whose intensities were considered as extreme outliers, were omitted from the final refinement. Refinement of the absolute structure parameter [21] for **15'** yielded a value of 0.44(10), which indicates that the crystals are most likely inversion twins. Neutral atom scattering factors for non-H-atoms were taken from [22a], and the scattering factors for H-atoms were taken from [23]. Anomalous dispersion effects were included in F_c [24]; the values for f' and f'' were those of [22b]. The values of the mass attenuation coefficients are those of [22c]. All calculations were performed using SHELXL97 [25] program.

[8]) CCDC- -contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Center via* http://www.ccdc.cam.ac.uk/data_request/cif.

Table. *Crystallographic Data of Compounds* **15** *and* **15'**

	15	**15'**
Crystallized from	hexane/CH_2Cl_2	hexane/CH_2Cl_2
Empirical formula	$C_{22}H_{24}ClN_3OS$	$C_{22}H_{24}ClN_3OS$
Formula weight [g mol-1]	413.96	413.96
Crystal color, habit	yellow, prism	colorless, needle
Crystal dimensions [mm]	0.30 × 0.32 × 0.35	0.05 × 0.08 × 0.22
Temperature [K]	160(1)	160(1)
Crystal system	triclinic	orthorhombic
Space group	$P, \bar{1}$	$P2_12_12_1$
Z	2	4
Reflections for cell determination	16212	173390
2θ range for cell determination [°]	4 – 60	4 – 50
Unit cell parameters a [Å]	10.0771(2)	7.1060(2)
b [Å]	10.3993(2)	12.4905(4)
c [Å]	11.3362(2)	23.3874(8)
α [°]	77.840(1)	90
β [°]	65.069(1)	90
γ [°]	85.567(1)	90
V [Å^3]	1053.02(4)	2075.8(1)
D_x [g cm^{-3}]	1.305	1.324
μ(MoK_α) [mm^{-1}]	0.298	0.302
Scan type	ϕ and ω	ϕ and ω
2θ (max) [°]	60	50
Transmission factors (min; max)	0.761; 0.915	0.794; 1.002
Total reflections measured	27147	29663
Symmetry-independent reflections	6137	3662
Reflections with $I > 2\sigma(I)$	5049	3178
Reflections used in refinement	6131	3662
Parameters refined; restraints	276; 48	258
Final $R(F)$ [$I > 2\sigma(I)$ reflections]	0.0465	0.0518
$wR(F^2)$ (all data)	0.1270	0.1192
Weighting parameters (a; b)[a]:	0.0645; 0.353	0.0458; 1.7391
Goodness of fit	1.062	1.130
Secondary extinction coeff.	0.27(1)	0.025(2)
Final Δ_{max}/σ	0.001	0.001
$\Delta\rho$(max; min) [e Å^{-3}]	0.51; -0.45	0.25; -0.27

[a]) $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$ where $P = (F_o^2 + 2F_c^2)/3$

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